Decision Memo for Magnetic Resonance Imaging (MRI) (CAG-00399R2)

Decision Summary

The Centers for Medicare & Medicaid Services (CMS) has determined that the evidence is not adequate to conclude that the use of magnetic resonance imaging (MRI) improves health outcomes for Medicare beneficiaries with implanted permanent pacemakers (PMs) or implantable cardioverter defibrillators (ICDs), and thus we determine that it is not reasonable and necessary under §1862(a)(1)(A) of the Social Security Act (the Act). Therefore, subject to one exception, we will retain the current general contraindications at Chapter 1, Section 220.2.C.1 in the NCD Manual.

CMS believes that the evidence is promising although not yet convincing that MRI will improve patient health outcomes if certain safeguards are in place to ensure that the exposure of the device to an MRI environment adversely affects neither the interpretation of the MRI result nor the proper functioning of the implanted device itself. We believe that specific precautions (listed below) could maximize benefits of MRI exposure for beneficiaries enrolled in clinical studies designed to assess the utility and safety of MRI exposure. Therefore, CMS determines that MRI will be covered by Medicare when studied in a clinical study under § 1862(a)(1)(E) (consistent with § 1142 of the Act) if the study meets the criteria in each of the three paragraphs below.

The approved prospective clinical study must, with appropriate methodology, address one or more aspects of the following questions:

1. Do results of MRI in PM/ICD beneficiaries with implanted cardiac devices affect physician decision making related to:
   a. Clinical management strategy (e.g., in oncology, toward palliative or curative care);
   b. Planning of treatment interventions; or
   c. Prevention of unneeded diagnostic studies or interventions, or preventable exposures?
2. Do results of MRI in PM/ICD beneficiaries with implanted cardiac devices affect patient outcomes related to:
   a. Survival;
   b. Quality of life; or
   c. Adverse events during and after MR scanning?

In addition, the prospective clinical study of MRI must include safety criteria for all participants. Such required safety measures for such studies, as further explained in guidance documents from professional societies (e.g., Kanal et al., 2007; Levine et al., 2007), must include but are not limited to:

1. MRI should be done on a case-by-case and site-by-site basis.

2. MRI scan sequences, field intensity, and field(s) of exposure should be selected to minimize risk to the patient while gaining needed diagnostic information for diagnosis or for managing therapy.
3. MRI scanning should be done only if the site is staffed with individuals with the appropriate radiology and cardiology knowledge and expertise on hand.
4. Implanted device patients who are candidates for recruitment for an MRI clinical study should be advised that life-threatening arrhythmias might occur during MRI and serious device malfunction might occur, requiring replacement of the device.
5. Radiology and cardiology personnel and a fully stocked crash cart be readily available throughout the procedure in case a significant arrhythmia develops during the examination that does not terminate with the cessation of the MR study. The cardiologist should be familiar with the patient's arrhythmia history and the implanted device. A programmer that can be used to adjust the device as necessary should be readily available.
6. All such patients should be actively monitored for cardiac and respiratory function throughout the examination. At a minimum, ECG and pulse oximetry should be used. Visual and verbal contact with the patient must be maintained throughout the MRI scan. The patient should be instructed to alert the MRI staff on hand to any unusual sensations, pains, or to any problems.
7. At the conclusion of the examination, the cardiologist should examine the device to confirm that the function is consistent with its preexamination state.
8. Follow-up should include a check of the patient's device at a time remote (1–6 weeks) after the scan to confirm appropriate function.
9. If the implanted device manufacturer has indicated additional safety precautions appropriate for safe MRI performance, these must be included in the study protocol.

The clinical study must adhere to the following standards of scientific integrity and relevance to the Medicare population.

a. The principal purpose of the research study is to test whether a particular intervention potentially improves the participants' health outcomes.
b. The research study is well supported by available scientific and medical information or it is intended to clarify or establish the health outcomes of interventions already in common clinical use.
c. The research study does not unjustifiably duplicate existing studies.
d. The research study design is appropriate to answer the research question being asked in the study.
e. The research study is sponsored by an organization or individual capable of executing the proposed study successfully.
f. The research study is in compliance with all applicable Federal regulations concerning the protection of human subjects found at 45 CFR Part 46. If a study is regulated by the Food and Drug Administration (FDA), it must be in compliance with 21 CFR Parts 50 and 56.
g. All aspects of the research study are conducted according to appropriate standards of scientific integrity (see http://www.icmje.org).
h. The research study has a written protocol that clearly addresses, or incorporates by reference, the standards listed here as Medicare requirements for coverage with evidence development (CED).
i. The clinical research study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Trials of all medical technologies measuring therapeutic outcomes as one of the objectives meet this standard only if the disease or condition being studied is life threatening as defined in 21 CFR § 312.81(a) and the patient has no other viable treatment options.
j. The clinical research study is registered on the ClinicalTrials.gov website by the principal sponsor/investigator prior to the enrollment of the first study subject.
k. The research study protocol specifies the method and timing of public release of all prespecified outcomes to be measured including release of outcomes if outcomes are negative or study is terminated early. The results must be made public within 24 months of the end of data collection. If a report is planned to be published in a peer reviewed journal, then that initial release may be an abstract that meets the requirements of the International Committee of Medical Journal Editors (http://www.icmje.org). However a full report of the outcomes must be made public no later than three (3) years after the end of data collection.
l. The research study protocol must explicitly discuss subpopulations affected by the treatment under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion criteria effect enrollment of these populations, and a plan for the retention and reporting of said populations on the trial. If the inclusion and exclusion criteria are expected to have a negative effect on the recruitment or retention of underrepresented populations, the protocol must discuss why these criteria are necessary.

m. The research study protocol explicitly discusses how the results are or are not expected to be generalizable to the Medicare population to infer whether Medicare patients may benefit from the intervention. Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability or Medicaid eligibility.

Consistent with section 1142 of the Act, the Agency for Healthcare Research and Quality (AHRQ) supports clinical research studies that CMS determines meet the above-listed standards and address the above-listed research questions.

Back to Top

Decision Memo

TO: Administrative File CAG-00399R2
FROM:

Louis B. Jacques, MD
Director, Coverage and Analysis Group

Tamara Syrek Jensen, JD
Deputy Director, Coverage and Analysis Group

James Rollins, MD, PhD
Director, Division of Items and Devices

Brijet Burton, MPP, MS, PA-C
Lead Analyst, Division of Items and Devices

Sarah Meisenberg
Analyst, Division of Items and Devices

Leslye Fitterman, PhD

Epidemiologist, Analyst, Division of Items and Devices

Rosemarie Hakim, PhD
Epidemiologist, Division of Operations and Information Management

Jeffrey C. Roche, MD, MPH
Medical Officer, Division of Items and Devices

SUBJECT: Final Decision Memorandum of Magnetic Resonance Imaging
DATE: February 24, 2011

I. Final Decision:

The Centers for Medicare & Medicaid Services (CMS) has determined that the evidence is not adequate to conclude that the use of magnetic resonance imaging (MRI) improves health outcomes for Medicare beneficiaries with implanted permanent pacemakers (PMs) or implantable cardioverter defibrillators (ICDs), and thus we determine that it is not reasonable and necessary under §1862(a)(1)(A) of the Social Security Act (the Act). Therefore, subject to one exception, we will retain the current general contraindications at Chapter 1, Section 220.2.C.1 in the NCD Manual.

CMS believes that the evidence is promising although not yet convincing that MRI will improve patient health outcomes if certain safeguards are in place to ensure that the exposure of the device to an MRI environment adversely affects neither the interpretation of the MRI result nor the proper functioning of the implanted device itself. We believe that specific precautions (listed below) could maximize benefits of MRI exposure for beneficiaries enrolled in clinical studies designed to assess the utility and safety of MRI exposure. Therefore, CMS determines that MRI will be covered by Medicare when studied in a clinical study under § 1862(a)(1)(E) (consistent with § 1142 of the Act) if the study meets the criteria in each of the three paragraphs below.

The approved prospective clinical study must, with appropriate methodology, address one or more aspects of the following questions:

1. Do results of MRI in PM/ICD beneficiaries with implanted cardiac devices affect physician decision making related to:
   a. Clinical management strategy (e.g., in oncology, toward palliative or curative care);
   b. Planning of treatment interventions; or
   c. Prevention of unneeded diagnostic studies or interventions, or preventable exposures?
2. Do results of MRI in PM/ICD beneficiaries with implanted cardiac devices affect patient outcomes related to:

a. Survival;
b. Quality of life; or
c. Adverse events during and after MR scanning?

In addition, the prospective clinical study of MRI must include safety criteria for all participants. Such required safety measures for such studies, as further explained in guidance documents from professional societies (e.g., Kanal et al., 2007; Levine et al., 2007), must include but are not limited to:

1. MRI should be done on a case-by-case and site-by-site basis.
2. MRI scan sequences, field intensity, and field(s) of exposure should be selected to minimize risk to the patient while gaining needed diagnostic information for diagnosis or for managing therapy.
3. MRI scanning should be done only if the site is staffed with individuals with the appropriate radiology and cardiology knowledge and expertise on hand.
4. Implanted device patients who are candidates for recruitment for an MRI clinical study should be advised that life-threatening arrhythmias might occur during MRI and serious device malfunction might occur, requiring replacement of the device.
5. Radiology and cardiology personnel and a fully stocked crash cart be readily available throughout the procedure in case a significant arrhythmia develops during the examination that does not terminate with the cessation of the MR study. The cardiologist should be familiar with the patient's arrhythmia history and the implanted device. A programmer that can be used to adjust the device as necessary should be readily available.
6. All such patients should be actively monitored for cardiac and respiratory function throughout the examination. At a minimum, ECG and pulse oximetry should be used. Visual and verbal contact with the patient must be maintained throughout the MRI scan. The patient should be instructed to alert the MRI staff on hand to any unusual sensations, pains, or to any problems.
7. At the conclusion of the examination, the cardiologist should examine the device to confirm that the function is consistent with its preexamination state.
8. Follow-up should include a check of the patient's device at a time remote (1–6 weeks) after the scan to confirm appropriate function.
9. If the implanted device manufacturer has indicated additional safety precautions appropriate for safe MRI performance, these must be included in the study protocol.

The clinical study must adhere to the following standards of scientific integrity and relevance to the Medicare population.

a. The principal purpose of the research study is to test whether a particular intervention potentially improves the participants' health outcomes.
b. The research study is well supported by available scientific and medical information or it is intended to clarify or establish the health outcomes of interventions already in common clinical use.
c. The research study does not unjustifiably duplicate existing studies.
d. The research study design is appropriate to answer the research question being asked in the study.
e. The research study is sponsored by an organization or individual capable of executing the proposed study successfully.
f. The research study is in compliance with all applicable Federal regulations concerning the protection of human subjects found at 45 CFR Part 46. If a study is regulated by the Food and Drug Administration (FDA), it must be in compliance with 21 CFR Parts 50 and 56.
g. All aspects of the research study are conducted according to appropriate standards of scientific integrity (see http://www.icmje.org).
h. The research study has a written protocol that clearly addresses, or incorporates by reference, the standards listed here as Medicare requirements for coverage with evidence development (CED).
i. The clinical research study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Trials of all medical technologies measuring therapeutic outcomes as one of the objectives meet this standard only if the disease or condition being studied is life threatening as defined in 21 CFR § 312.81(a) and the patient has no other viable treatment options.

j. The clinical research study is registered on the ClinicalTrials.gov website by the principal sponsor/investigator prior to the enrollment of the first study subject.

k. The research study protocol specifies the method and timing of public release of all prespecified outcomes to be measured including release of outcomes if outcomes are negative or study is terminated early. The results must be made public within 24 months of the end of data collection. If a report is planned to be published in a peer reviewed journal, then that initial release may be an abstract that meets the requirements of the International Committee of Medical Journal Editors (http://www.icmje.org). However a full report of the outcomes must be made public no later than three (3) years after the end of data collection.

l. The research study protocol must explicitly discuss subpopulations affected by the treatment under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion criteria effect enrollment of these populations, and a plan for the retention and reporting of said populations on the trial. If the inclusion and exclusion criteria are expected to have a negative effect on the recruitment or retention of underrepresented populations, the protocol must discuss why these criteria are necessary.

m. The research study protocol explicitly discusses how the results are or are not expected to be generalizable to the Medicare population to infer whether Medicare patients may benefit from the intervention. Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability or Medicaid eligibility.

Consistent with section 1142 of the Act, the Agency for Healthcare Research and Quality (AHRQ) supports clinical research studies that CMS determines meet the above-listed standards and address the above-listed research questions.

II. Background Information

As noted in prior NCDs on this topic, an MRI "(formerly known as nuclear magnetic resonance imaging - NMRI) is a noninvasive method of graphically representing the distribution of water and other hydrogen-rich molecules in the human body." MRI is a diagnostic imaging modality that is capable of demonstrating a wide variety of soft-tissue lesions with contrast resolution equal or superior to CT scanning in various parts of the body. Among its advantages are the absence of ionizing radiation and the ability to achieve high levels of tissue contrast resolution without injected iodinated radiological contrast agents.

However, MRI exposes the patient to strong magnetic fields which may cause the movement or heating of implanted medical devices that are ferromagnetic (e.g. surgical clips) or that have ferromagnetic components (e.g. pacemakers, prostheses.) The American College of Radiology (ACR's) guidance document on safe MR Practices (Kanal 2007) explicitly speaks to the need to address the possibility that the patient may have ferromagnetic foreign bodies or implants.

Authors have described the effects of intense and high-frequency magnetic fields on ferromagnetic or conducting objects. For example, a review of pacemaker malfunction (Hayes and Vlietstra, 1993) notes that "… exposure to MRI causes pacemakers to revert to an asynchronous mode (in which impulse generation by the pacemaker occurs at a fixed rate, independent of underlying cardiac activity). This effect can be avoided only in PMs in which the magnet response can be programmed 'off'." The review's authors suggested use of other techniques to allow safe MR scanning of non-PM-dependent patients. These authors also note that "… [i]f the body area to be imaged is in close proximity to the pacemaker site, the pacemaker-induced artifact on MRI may obscure the images."

A later review article (Schoenfeld, 2007) states that "…(p)otential interactions (of PMs) with MRI include pacing inhibition, inappropriate ICD discharges, rapid pacing, mechanical pull and rotation of the device, and device reprogramming," and suggests strategies to improve safety of MR scanning for patients with PMs and ICDs: "…Certain strategies to minimize complications have been suggested, including the use of less powerful MRI machines; imaging limited to extremities (i.e., remote from the implanted device); careful reprogramming of the intracardiac device, including asynchronous modes and maximal pacing output; selection of appropriate spin sequences; limitation of MRI to patients who are not pacemaker dependent; and careful, continuous periprocedure monitoring."

III. History of Medicare Coverage

Section 220.2 of Chapter 1 of the Medicare National Coverage Determination (NCD) Manual provides coverage of MRI for a number of clinical indications. Coverage is limited to MRI instruments that have received FDA premarket approval, and such units must be operated within the parameters specified by the approval.

In addition (and as noted by the requester), payment for an MRI examination is not currently covered by Medicare if certain contraindications are present. These include cardiac PMs (as indicated in the following section of the Medicare NCD Manual, Chapter 1, Section 220.2.C.1, as downloaded by CMS staff on November 2, 2010):

C. Contraindications and Nationally Non-Covered Indications

1. Contraindications

"The MRI is not covered when the following patient-specific contraindications are present:

• It is not covered for patients with cardiac pacemakers or with metallic clips on vascular aneurysms.

• MRI during a viable pregnancy is also contraindicated at this time.

• The danger inherent in bringing ferromagnetic materials within range of MRI units generally constrains the use of MRI on acutely ill patients requiring life support systems and monitoring devices that employ ferromagnetic materials. …
(Source: Medicare On-line NCD Manual, available at www.cms.hhs.gov).

Specific conditions for Medicare coverage of MRI, including deletion of prior contraindications, have changed during the past 25 years. In November 1985, CMS first set forth the conditions under which MRI may be covered. Subsequent policy revisions in 1988, 1991, and 1994 provided MRI coverage under Medicare for additional conditions. Currently covered indications for MRI include examination of the head, central nervous system, and spine. MRI can also assist in the differential diagnosis of mediastinal and retroperitoneal masses, including abnormalities of the large vessels such as aneurysms and dissections. MRI may also be used to detect and stage pelvic and retroperitoneal neoplasms and to evaluate disorders of cancellous bone and soft tissues. MRI may also be covered to diagnose disc disease without regard to whether radiological imaging has been tried first to diagnose the problem. Most recently, a 2009 NCD removed a contraindication from 220.2.C.2 concerning blood flow measurement. Other uses of MRI for which CMS has not specifically indicated national coverage are under local contractor discretion.

A. Current Request for Reconsideration

CMS received a letter dated June 25, 2010 from Dr. Robert J. Russo, MD, PhD, FACC, Scripps Clinic, LaJolla, California requesting reconsideration of Section 220.2's contraindications for MRI. The requester asked that the current Medicare coverage for MRI be changed, both to remove a contraindication for patients who undergo MRI and who had implanted PMs, as well as to provide Medicare coverage for patients who undergo MRI and who had implanted ICDs, if (1) a clinically-indicated MRI is performed as part of a prospective clinical study designed to determine the risk of the procedure, and (2) the study is conducted after an IDE has been approved by FDA for a device involved in the proposed research.

The requester's concerns can be summarized as follows.

1. Millions of patients in the United States currently have implanted pacemakers or other devices.
2. The estimated lifetime risk of requiring an MRI is 50-75% (Requester's reference #4).
3. Medicare currently contraindicates coverage of MRI in patients with implanted pacemakers.
4. In the absence of Medicare coverage, beneficiaries for whom MRI is the most appropriate diagnostic imaging modality may be denied access to MRI.
5. Absent an exception to the existing contraindication to MRI coverage in patients with implanted pacemakers, clinical trials to determine safety may be infeasible.

B. Benefit Category

Medicare is a defined benefit program. An item or service must fall within a benefit category as a prerequisite to Medicare coverage §1812 (Scope of Part A); §1832 (Scope of Part B) and §1861(s) (Definition of Medical and Other Health Services) of the Act. Magnetic resonance imaging is considered to be within the following benefit category: other diagnostic tests §1861(s)(3).

Medicare regulations at 42 CFR 410.32(a) state in part, that "…diagnostic tests must be ordered by the physician who is treating the beneficiary, that is, the physician who furnishes a consultation or treats a beneficiary for a specific medical problem and who uses the results in the management of the beneficiary's specific medical problem." Thus, except where other uses have been explicitly authorized by statute, Medicare does not cover MRI for routine screening or surveillance.

IV. Timeline of Recent Activities

June 28, 2010	The request letter and list of references was sent by Dr. Russo to CMS. CMS posts a tracking sheet and opens a National Coverage Reconsideration to determine if there is sufficient evidence to change the policy. The initial 30-day public comment period begins.
July 28, 2010	Initial public comment period ended. CMS received a total of 3 comments.
December 1, 2010	CMS posts the proposed decision memorandum for 30 days of public comment period.
December 31, 2010	The public comment period on the proposed decision memo closes with five public comments received.

V. FDA Status

We note that the FDA status of the MRI scanner was not a specific issue raised by the requester.

FDA approved the first pacemaker (Medtronic Revo MRI SureScan™ Pacing System) for use during certain MRI exams on February 8, 2011. This approval came after the public comment period, required by section 1862(l) of the Act, and was too late for CMS to adequately review the evidence to address coverage for MRI for patients that may obtain this device.

VI. General Methodological Principles

When making NCDs, CMS normally evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service falling within a benefit category is reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. The critical appraisal of the evidence enables us to determine to what degree we are confident that: 1) the specific assessment questions can be answered conclusively; and 2) the intervention will improve health outcomes for beneficiaries. An improved health outcome is one of several considerations in determining whether an item or service is reasonable and necessary.

Public commenters sometimes cite the published clinical evidence and provide CMS with useful information. Public comments that provide information based on unpublished evidence, such as the results of individual practitioners or patients, are less rigorous and, therefore, less useful for making a coverage determination. CMS uses the initial comment period to inform the public of its proposed decision. CMS responds in detail to the public comments that were received in response to the proposed decision when it issues the final decision memorandum.

VII. Evidence

Below is a summary of the evidence we reviewed. CMS may consider published articles submitted by the requester either as sources of evidence, or for background and general information. Though we reconsidered MRI in 2009, the underlying questions are different in this reconsideration and thus we are considering a broader body of evidence this time.

A. Introduction

A review article (Nazarian and Halperin 2009) summarizes the findings of eight clinical studies, published from 1996 - 2006, of effects of clinical MR scans in patients with PMs or ICDs. A total of 31 patients with ICDs and 261 patients with PMs underwent MR scanning with field strengths from 0.5 to 2.0 T. It was noted that: some electrical characteristics of the PM or ICD may change after MR scans; PM reprogramming was needed in less than 2% of patients in one study; and occasional device-associated artifacts were noted on MRI images. Some studies used special 'safety' protocols to avoid MR scan interference with device function, as well as close patient monitoring during the scan.

Any of these effects of MRI on an implanted cardiac device might affect the patient's health outcomes, especially among patients who depend on the device to monitor and (if needed) correct an aberrant heart rhythm, e.g., to recognize and stop ventricular fibrillation (VF), an extremely serious arrhythmia. The American Heart Association (AHA) (Levine 2007) recognized the challenges of safe MR scanning in patients with implanted electrically active cardiac devices and/or with ferromagnetic foreign bodies or implants, among others.

In addition to the risk of MR scanning to change PM or ICD function, the presence of metallic implanted devices can affect the accuracy of MR images. The Nazarian and Halperin 2009 article mentions reports of several types of such artifacts, including image distortion, signal voids or bright areas, and poor fat suppression. According to these authors, such image artifacts are more pronounced in certain types of MR examinations, including inversion recovery and steady-state free precession sequences. Such misleading artifacts may, in certain imaging applications such as cardiac MRI, suggest scarring or other tissue abnormalities, and lead to misinterpretation. However, according to these authors, such artifacts can be reduced by advance planning, patient positioning and scan processing adjustments.

We opened this NCA to review the evidence on the use of MRI in patients who have implanted PM or ICD devices. This NCA does not focus on the use of MRI for any particular indication, i.e., for any specific disease(s) or condition(s).

B. Discussion of Evidence Reviewed

1. Questions

In assessing the evidence regarding this topic, CMS formulated two questions similar to those used in prior decisions relating to this topic area (for example, in the decision memorandum regarding the initial reconsideration for MRI, CAG-00399R (September 2009)).

Q1. Is there adequate evidence to conclude that MRI performed for clinically appropriate imaging indications informs the diagnosis or clinical management decisions in patients with implanted PMs or ICDs?

Q2. Is there adequate evidence to conclude that MRI performed for clinically appropriate imaging indications improves health outcomes in patients with implanted PMs or ICDs?

We recognize that improvements in health outcomes may arise from changes in physician management of the patient's condition, brought about through thoughtful consideration of the results of diagnostic testing. We also searched for indications in qualifying clinical studies of safety concerns or adverse events in participants with implanted devices undergoing MRI. We considered this prudent in view of known adverse events to which subjects might be vulnerable.

As has been done in other decisions, CMS considered the evidence in the hierarchical framework of Fryback and Thornbury (1991) where Level 2 addresses diagnostic accuracy, sensitivity, and specificity of the test; Level 3 focuses on whether the information produces change in the physician's diagnostic thinking; Level 4 concerns the effect on the patient management plan and Level 5 measures the effect of the diagnostic information on patient outcomes.

2. External Technology Assessments

CMS did not request an external technology assessment (TA) on this issue.

3. Internal Technology Assessment

Articles submitted by the requestor:

Prospective Case Series

Del Ojo JL, Moya F, Villalba J, et al. Is magnetic resonance imaging safe in cardiac pacemaker recipients? *Pacing & Clinical Electrophysiology.* Apr 2005; 28(4): 274-278.

The stated purpose of this prospective case series study was to evaluate the safety of MRI. Participants included 13 subjects (10 males and 3 females), ranging in age from 59 to 79 years, with a median age of 71 years. Inclusion criteria were: patients had to have an implanted PM (Affinity ™ DR model 5330 PMs (St. Jude Medical) connected to a Tendril ™ model 1388 leads (St. Jude Medical)), and a clinical indication for MRI. Among these thirteen patients, the indications for PM implantation included sinus node disease (n = 7) and atrioventricular block (n=6).

Prior to MRI, all patients displayed a stable spontaneous rhythm and were not considered PM-dependent. The study's three objectives were to (1) reassess risks of performing an MR scan in PM patients; (2) compare pacing functions before and after the exposure to the MR environment; and (3) monitor the development of possible adverse effects. During MR scanning, stimulation and sensing polarity were programming to bipolar for each PM. Sensor, magnet and AutoCapture™ functions were programmed off, and other PM functions were allowed to remain enabled if originally enabled in that patient's device. Outcomes of interest included both (1) pre- to post-MR scan changes in electrical characteristics of PM; and (2) occurrence of any adverse events during or after MRI in patients with PM, based on post-MR interviews with patients and on post-MR interrogation of the PM.

Results of the study revealed the absence of PM inhibition, asynchronous pacing, or inappropriately rapid pacing. Each patient underwent thoracic MRI at 2.0 T. Eight patients also underwent head (n = 3); cervical spine (n = 2); neck (n = 2); and lumbar spine (n = 1) scanning in addition to the thoracic MR scan. During the study, no patient reported discomfort, heat, or motion sensation at the PM implant site. And based on post-MR scan interrogation of the PM function, there were no significant differences in the sensing, stimulation, AutoCapture™ threshold, and lead impedance measurements before and after MR scans. The authors concluded that performing 2.0 T-MR scans in patients with Affinity ™ DR model 5330 PM connected to a Tendril ™ model 1388 lead is safe.

Gimbel JR, Johnson D, Levine PA, et al. Safe performance of MRI on five patients with permanent cardiac PMs. Pacing Clin Electrophysiol 1996; 19(6): 913-9.

The purpose of this prospective case series study was to evaluate a strategy to allow safe MR scan in patients with implanted PMs. Five patients, whose age and gender information were not provided, all had implanted PMs of different models from a single manufacturer (Pacesetter, Sylmar, CA). Patients were eligible for the study if their physician had ordered an MR scan, for: brain or pituitary scan (n = 2); cervical disk (n = 1); heart valve (n = 1); or "CIA" (n = 1). One participant was described as 'PM dependent,' a condition defined as having an escape rhythm that was hemodynamically unstable. During the MR scan, patients were monitored using electrocardiogram (ECG) signals (n = 3), pulse oximetry (n=1), or by verbal contact with a nurse stationed nearby. A 'heavy dressing' was applied over the PM implant pocket in four patients, at the discretion of the attending physician, in order to minimize the torque effect for patient comfort. The study was designed to also include a post-MR scan, in which the PM was interrogated and device reprogramming would be performed at the discretion of the attending physician.

Follow-up at three months post-MR scan would also be performed to assess capture and sensing thresholds. Results of the study revealed that MR scans were conducted at between 0.35 – 1.5 T. When questioned about any sensations noted during the MR scan one patient noted that her "heart stopped beating toward the end of the scan." No twisting or heating sensations or any other unusual symptoms were reported during or immediately after MR scans. Pre-MR scan, the PM was interrogated. No changes occurred to the programmed or measured parameters of the devices tested. Pacing and sensing thresholds remained the same as those recorded before the MR scan. In the only patient for whom the device's event record was available, normal pacemaker function was noted during the scan. MR image results from four out of five patients were described as 'excellent.' However, in one case, artifact from the PM 'compromised' the MR image for evaluating the patient's cardiac valve. The authors concluded that "(w)hen appropriate strategies are used our experience suggests that MRI may be performed, when necessary, with an acceptable risk / benefit ratio to the patient."

Naehle CP, Strach K, Thomas D, et al. Magnetic Resonance Imaging at 1.5-T in Patients With Implantable Cardioverter-Defibrillators. J Am Coll Cardiol 2009; 54: 549–55.

The purpose of this prospective case series was to evaluate a strategy for safe performance of MR scanning at 1.5 T. The study included 18 patients who had been implanted with ICDs for at least three months prior to enrolling in the study. The patients' mean age was 61.8 years (range: 35-84 years); gender information was not provided. Inclusion criteria included: (1) urgent need for an MRI examination; (2) presence of an ICD system, with at least six months' estimated battery life; (3) pacing lead impedances 200 to 2,000 ohms; (4) shock lead impedance 10 to 80 ohms; (5) stable pacing parameters: pacing capture threshold < 2.5 V at a pulse duration of 0.4 ms; sensing > 5 mV; and (6) a minimum of three months since ICD and lead implantation.

Exclusion criteria included: (1) unstable angina; (2) myocardial infarction or cardiothoracic surgery within the previous three months; (3) pacemaker dependency (defined as an intrinsic heart rate less than 50 beats/min); (4) presence of MRI incompatible bioimplants or other MRI incompatible materials, or presence of abandoned leads. The manufacturers of the implanted ICDs in these patients were: Medtronic (n = 8); Guidant (n = 4); Biotronik (n = 3); and other (n = 3). The protocol evaluated consisted of reprogramming of ICD pre-MR scan, as per protocol; 1.5 T MR scan; patient symptom report during MR scan; pre- and post-scan sampling of patient troponin level; pre- and post-scan ICD interrogation; ICD reprogramming post-MR to baseline; and three month follow-up.

Results of the study revealed absence of any of the following: MR scan termination; patient-reported sensations; heart rate or rhythm variations or arrhythmias; or electrical reset of ICDs. For troponin levels, there was no significant pre- to post-MR scan change by Student's T test, and there was no elevation above the indicated upper limit of the reference interval (i.e., 0.1 ng/mL). Finally, two parameters were reported to change significantly (by the Wilcoxon signed rank test) in the pre-MR scan to post-MR scan comparisons: (1) mean battery voltage ("3.86 +/- 1.48 Volts ('V') pre-MR to 3.83 +/- 1.48 V post-MR"); and (2) mean capacitor charging time (from 11.2 +/- 4.9 seconds pre-MR scan to 9.5 +/- 4.28 seconds post-MR scan) (all from Table 4)). The authors concluded that "MRI of non–pacemaker-dependent ICD patients can be performed with an acceptable risk/benefit ratio under controlled conditions by taking both MRI- and pacemaker-related precautions."

Nazarian S, Bluemke DA, Lardo AC, et al. Clinical Utility and Safety of a Protocol for Noncardiac and Cardiac MRI of Patients With PMs and ICDs at 1.5 Tesla. Circulation. 2006; 114: 1277-84.

In this prospective case series involving 55 patients, the authors assessed the immediate and long-term safety of MRI protocol for patients with permanent PM or ICD and the diagnostic yield of MRI in this setting. Thirty-one of the 55 patients had an implanted PM (with 12 of the 31 PM-dependent) and 24 of the 55 had an implanted ICD. Age and gender information about participants was not provided. Inclusion criteria included any clinical indication for MRI with no acceptable imaging alternative and an implanted cardiac device if the PM or ICD had been found to be safe by previous in vitro phantom and in vivo animal testing. Exclusion criteria were patients with device implantation less than six weeks before MRI and patients with nontransvenous epicardial leads, no fixation (such as superior vena cava coil), or abandoned leads.

The 55 enrollees underwent a total of 68 MR scans. The main outcomes of interest included: changes in electrical characteristics of PMs, ICDs and ability of MR scan images to answer clinical questions pertaining to diagnostic yield. All patients underwent at least one MR scan with safety protocol and concurrent monitoring. For each scan, pre- and post-scan interrogations of implanted devices and long-term follow-up were performed. In addition, images from MR scans were reviewed. Results of the study revealed: (1) no symptoms consistent with device movement, torque, or heating were reported during MRI examinations; (2) no inappropriate inhibition of pacing was observed during MRI. In ten patients with permanent PMs without magnet-mode programming capability, reed switch activation by the static magnetic field of MR scanning led to transient asynchronous pacing at the device-specific magnet rate (85 pulses/minute), which ceased on patient positioning in the magnet bore; (3) no unexpected or rapid activation of pacing was observed during MR scanning; (4) all devices were functioning appropriately after MR scans, and no changes in device programming were observed; (5) twenty-nine of the participants had chronic device interrogation with median follow-up time of 99 days. No significant differences in device parameters were found at follow-up; and (6) answers to clinical questions were successfully determined in 27 of 29 (93%) thoracic MR scans, and in all 39 (100%) non-thoracic MR scans.

The authors concluded that "…MRI can be performed safely in patients with certain permanent pacemaker or ICD systems. When proper precautions are taken, MRI of the region that contains the device is not associated with increased risk. This ability may significantly impact clinical decision making in appropriate patients..." The authors also commented that (1) transient reed switch activation, a part of normal device function, has minimal to no clinical consequences; and that (2) no cardiac devices had (as of 2006) achieved industry or FDA clearance for MR scanning compatibility, and catastrophic complications have been reported.

Sommer T, Naehle CP, Yang A, et al. Strategy for Safe Performance of Extrathoracic MRI at 1.5 Tesla in the Presence of Cardiac PMs in Non–PM-Dependent Patients: A Prospective Study With 115 Examinations. Circulation. 2006 Sep 19; 114: 1285-92.

The purpose of this prospective consecutive case series study is to evaluate a strategy for safe performance of extra-thoracic MRI in non-PM-dependent patients with cardiac PMs. After reviewing potential candidates, only 82 subjects met the inclusion/exclusion criteria. They underwent a total of 115 MR scans at 1.5 T. Patients' mean age was 66.9 years (range 4 – 89 years); 53 males (65%) and 29 females (35%) participated. Inclusion criteria for the study included the presence of a cardiac PM and an urgent clinical need for MRI. Exclusion criteria were PM-dependent patients and those patients requiring examination of the thoracic region, as well as presence of MR scan-incompatible bioimplants or other materials.

Various models of Medtronic PMs, and various models of atrial and ventricular leads from a variety of manufacturers (Medtronic, Guidant, Biotronik, St. Jude Medical, etc.) were implanted in participants. All PMs were reprogrammed before MR scanning based on pre-scan pulse: if heart rate was < 60 bpm, the asynchronous mode was programmed to avoid MR–induced inhibition; if heart rate was > 60 bpm, sense-only mode was used to avoid MR-induced competitive pacing and potential proarrhythmia. During the MR scan, audio contact was established via an intercom system, and patients were asked to inform the investigator immediately of any torque or heating sensation, palpitations, dizziness, pain, or other unusual symptoms during imaging. An electrophysiologist and full resuscitation equipment were present during all examinations. Patients were monitored with ECG and pulse oximetry. To minimize radiofrequency-related lead heating, the specific absorption rate was limited to 1.5 W/kg. PMs were interrogated immediately before and after the MR scan and after three months, including measurement of pacing capture threshold (PCT) and serum troponin I levels.

Results of the study revealed: (1) all MR scans were completed safely; (2) inhibition of pacemaker output or induction of arrhythmias was not observed; (3) PCT increased significantly from pre- to post-MR scan (P = 0.017). In two of 195 leads, an increase in PCT was only detected at follow-up; (4) in four of 114 examinations, troponin increased from a normal baseline value to above normal after MR scan. In one case (troponin pre-MR scan 0.02 ng/mL, post-MR scan 0.16 ng/mL), this increase was associated with a 'significant' increase in PCT. The authors suggested that this increase in one patient might indicate myocardial injury; and (5) after MR scan, six patients died at a mean interval of 58 days (range 42 to 81 days) after MR scan. All deaths were related to the underlying disease (melanoma with cerebral metastases, pancreatic carcinoma, and brain tumors (n=4). None of the six deaths were classified as pacemaker or MR scan related. The authors concluded that extrathoracic MR scan of non–PM-dependent patients can be performed with an acceptable risk-benefit ratio under controlled conditions and by taking both MR- and PM-related precautions.

Case Series

Gimbel JR, Bailey SM, Tchou PJ, et al. (Gimbel 2005) Strategies for the Safe MRI of PM-Dependent Patients. Pacing Clin Electrophysiol. 2005; 28:1041–6.

In this case series, the authors' objective was to determine if strategies used to safely scan non-PM-dependent patients could be applied to facilitate safe MRI of PM-dependent patients. The authors defined pacemaker-dependence as the absence of an underlying escape rate below the lowest programmed rate of the device. Ten PM-dependent patients underwent eleven MR scans. Age and gender information were not provided. The protocol stipulated that patients could not undergo MRI until six weeks after PM implantation. PMs implanted in these ten patients included: Pacesetter (n=5); Medtronic (n=5), with PM leads from various manufacturers.

During MR scanning, the study's protocol for safety included: (1) screening, reprogramming and monitoring strategies were used to facilitate MR scan; (2) continuous pulse oximetry as well as electrocardiogram (EKG) monitoring was used to monitor the patients during the MR scans; (3) an electro-physiologist was present throughout each study; and (4) the electro-physiologist and the MR technologist remained in voice contact with the patient during each procedure. All patients in this study had MR scans limited to the head and neck using a transmit receive head coil on a Siemens 1.5 Tesla Vision whole-body MR machine. This head coil limits "…direct RF exposure to the IPG and its leads in the chest." Results of the study revealed: (1) all MR scans proceeded uneventfully. No difficulties in post-MR scan telemetry or interrogation were seen and no post-MR scan programming changes were noted; (2) no patient experienced arrhythmia or symptoms during or immediately after MR scan; (3) PM battery status remained unchanged; (4) no patient experienced post-MR scan change in sensing thresholds; and (5) three of ten patients showed no change in the atrial or ventricular pacing thresholds when the pre-MR scan values were compared to the immediate post-MR scan values and the three month follow-up values. The seven of the remaining ten patients showed a rise or fall of 0.5 V in their chamber pacing threshold values when the pre-MRI, post-MRI, and three month follow-up values were compared. In addition, all MR imaging studies produced diagnostic studies for the clinical question presented by the referring physicians.

The authors stated that "… [n]o clinically significant artifacts attributable to the pacemaker were identified within the field-of-view of the MR study." The authors concluded that "… (L)ike non-PM-dependent patients, MR scanning might be performed in PM-dependent patients if appropriate PM reprogramming, patient monitoring and MR scanning techniques are implemented."

Gimbel JR, Kanal E, Schwartz KM, et al.. Outcome of MRI in Selected Patients with Implantable Cardioverter Defibrillators (ICDs). Pacing Clin Electrophysiol. 2005; 28: 270–3.

In this case series, the authors studied seven patients with implanted ICDs and with medical reasons for MR scans, to determine if simple strategies used to safely scan PM patients could also be applied to ICD patients. Gender and age information about participants was not provided. Manufacturers of the seven implanted ICDs included Medtronic (n = 6) and Cardiac PaceMakers, Inc. (n = 1). Clinical indications for MR scans included suspected posterior fossa or pituitary tumor (n = 2); suspected brain metastases (n = 2); or other brain lesion or symptom (n =3). Reprogramming and monitoring strategies were used to facilitate MRI. Results of the study indicated that the seven patients underwent eight MR scans (one patient underwent pre- and post-op scan for a pituitary tumor).

In six of seven patients, during cranial MRI under continuous monitoring, no arrhythmias were noted, and no symptoms such as palpitations, tugging, or warmth were reported during the scan itself. In one of the patients one potentially serious adverse event occurred during a lumbar spine MR scan. The subject reported "painless involuntary muscle reaction like twitching several times" of his left upper pectoral region and upper extremity during the MR scan. This sensation stopped as the MR scan ended, and did not recur. This patient's device underwent a "Power On Reset" (POR) during MR scan. Post-MR scan communication with the device was unimpaired and all pacing, sensing, impedances, battery voltages, and charge times remained identical to the values obtained pre-MR scan. The manufacturer concluded that "the cause of the POR was due to a microprocessor instruction error and/or memory error," based on a personal communication with a reliability engineer employed by the manufacturer. Follow-up interrogation data at one month post-MR scan was available on six of seven patients. One patient expired ten days post-MR scanning from complications of metastatic lung cancer—metastatic brain lesions were seen only on MRI. No ICD dysfunction was noted prior to the patient's demise. At one month, the six ICDs available for analysis showed no change in pacing, sensing, impedance, battery voltage, or charge time parameters. The authors concluded that "Scanning of ICD patients might be performed if appropriate re-programming and monitoring is implemented."

Martin ET, Coman JA, Shellock FG, et al. MRI and Cardiac PM Safety at 1.5-Tesla. J Am Coll Cardiol 2004; 43: 1315–24.

In this mixed prospective-retrospective consecutive case series, the authors studied 54 patients with previously implanted PMs to determine if patients with PMs could safely undergo MRI at 1.5-Tesla. Each patient had a clinical indication for MR scan. PM-dependent patients were excluded from study participation. Excluding a scan for one patient in whom the PM was implanted at 'end-of-life,' performance of MR for the 61 other scans was evaluated. Gender and age information on participants was not provided. Seven of the 54 patients were included in the study prior to IRB approval of the study protocol and are included in the study analysis. Implanted PMs were the products of four different manufacturers, and each PM was interrogated immediately prior to MR scanning. MR scans (including MR angiography (MRA)) were performed at 1.5 Tesla. The types of MR scans included cardiac, vascular, and general MRI. No limitations were placed on the type or duration of the MRI procedure, PM, or lead models, nor proximity of the imaged anatomy relative to the PM.

During MR scans, patients were continuously monitored, and afterwards, PMs were interrogated. 'Any change' and 'any significant change' in pacing thresholds after MR were the outcomes of interest, and were reported as dichotomous variables as 'yes/no.' ('Any change' was determined in patients with any measurable difference in either an atrial or ventricular lead; 'any significant change' was determined with measurable differences exceeding 1 voltage or pulse width increment or decrement.) Also, changes in other electrical characteristics of PMs, including initial programming and lead impedances, as well as artifacts on MR images, were studied. Results of the study revealed: (1) no episodes of loss of capture or changes in lead impedances or battery voltages were noted after MR scans; (2) no damage to pacemaker circuits or movement of the pulse generator was observed; (3) no serious adverse events occurred. However, two patients reported 'mild and transient' symptoms; vibration (n = 1) and palpitations (n=1) coinciding "with inhibition of the pacing lead." Termination of MR procedure was not required in either case; (4) forty (37%) of 107 (48 atrial and 59 ventricular) leads underwent changes, whereas ten (9.4%) leads underwent a significant change; (5) two of 107 (1.9%) leads required a change in programmed output; and (6) threshold changes were unrelated to cardiac chamber, anatomical location, peak SAR, and time from lead implant to the MRI examination.

The authors concluded that safety was demonstrated in this series of patients with pacemakers at 1.5 T. They also discussed the clinical significance of the PM threshold changes observed. "Significant changes were infrequent … The energy increases that were needed to accommodate the rise in thresholds were minor and did not impair the safe performance of the pulse generators. Despite the labeling of these changes as significant, they were of no clinical consequence." The authors also noted that electro-magnetically induced noise, noted on telemetry, was monitored closely because it resembled serious cardiac arrhythmias.

Naehle CP, Volkert Z, Daniel T, et al. (Naehle et al., 2009B) Evaluation of Cumulative Effects of MR Imaging on Pacemaker Systems at 1.5 Tesla. Pacing Clin Electro-physiol. 2009; 32:1526–35.

In this retrospective case series, the authors evaluated possible cumulative effects of repeated MRI examinations on pacemaker systems in patients with cardiac pacemakers. The study population included 47 patients with PMs who underwent two or more MR examinations at 1.5 T in any anatomical region. These patients underwent a total of 171 MR scans, a median of two MR scans per patient; three patients underwent 12, 13, and 18 MR scans. Ages and gender information were not provided. Inclusion criteria included: (1) an urgent need for MRI; (2) stable physical PM parameters (estimated remaining battery lifetime >six months, LIs 200 to 2,000 ohms); (3) stable pacing parameters (PCT <.5 V at pulse duration of 0.4 ms, sensing > mV); and (4) three or more months since PM and lead implantation.

Exclusion criteria included: (1) absolute PM dependence (intrinsic heart rate less than 40 bpm); (2) presence of MRI-incompatible bioimplants or other MRI incompatible materials; and (3) history of ventricular tachycardia or VF. PMs from eight manufacturers had been implanted in the 47 study participants. Patients underwent different types of MR scans, including brain (n = 108); lumbar spine (n = 27); and other anatomical regions (n=38). To minimize the risk for RF related heating, the specific absorption rate was limited to 1.5 W/kg, and the scanning sequences were modified as necessary. Pacemakers were interrogated before and after MR scanning, and after 3 months; pacing captured threshold, lead impedance, while battery voltage were measured. PM electrical characteristics (e.g., pacing capture threshold) were compared using linear regression analysis for changes with the number of MR scans, and with time.

Results of the study revealed: (1) atrial pacing capture thresholds (PCT), both pre- and post-MR PCTs and PCT on three-month follow-up decreased by less than .01 volt (V) (C.I. -0.0193 - -0.0001) with increasing number of MR scans. None of the 37 patients with an atrial pacing lead had a change in PCT of 1.0 V or more; (2) based on data from 43 patients with ventricular pacing leads, both pre- and post-MRI and three-month follow-up, there was a small (-0.01- -0.02 V) decrease in ventricular PCT with increasing MR scans. None of these 43 patients had a change in ventricular PCT of 1.0 V or more; (3) lead impedance (LI) was not changed significantly based on number of MR scans. None of the patients' atrial or ventricular LI exceeded expected limits (200 – 2000 ohms); and (4) battery voltages (BV) showed a small but significant decrease as a function of number of MR scans received. In pre-MR, post-MR and follow-up the changes in BV were about 0.001 V/MR scan. However, these changes were less than the accuracy of the measurement. Also, mean BV decreased by 0.01V/year. The authors concluded that no clinically relevant, cumulative changes in PCT, LI, or BV could be detected in PM patients who underwent two or more MRI examinations. The authors suggested that further clinical studies of cumulative effects would be valuable.

Single Case Report

Naehle CP, Sommer T, Meyer C, et al. (Naehle 2006) "Strategy for Safe Performance of Magnetic Resonance Imaging on a Patient with ICD." Pacing Clin Electrophysiol 2006; 29: 113–6.

In this case report, the authors reported that an MR scan was performed on a 33 year old male patient with an ICD due to suspected recurrence of astrocytoma. The authors intended to demonstrate that full function of the ICD system was verified after imaging. Prior to MR scan, the ICD was interrogated for electrical characteristics, and a serum troponin level was drawn from the patient. An MR scan was performed at 1.5 T, with imaging and hardware protocols modified to minimize radiofrequency power deposition to the ICD device, a Biotronik Lexos VR ICD. During the MR scan, the patient was asked to report any sensations or symptoms. A complete ICD evaluation, to include electrical characteristics of ICD, measurement of sensing pacing capture thresholds (PCT), lead impedance, and battery voltage, would be performed immediately before and after the procedure, three days after and six weeks after the procedure. Also, post-scan serum troponin levels, and impact of MR results on patient's therapy were assessed.

The study results revealed the following: (1) the patient underwent the MR scan safely and without any discomfort, such as heating sensation or movement of the device. No cardiac arrhythmia was observed during the exam. (2) ICD interrogation immediately after MRI showed that no ventricular arrhythmia detection occurred, and that the ability to interrogate, program, or use telemetry was unaffected. The ICD did not undergo an electrical reset. PCTs remained stable, and other parameters showed only mild alterations, all within the margin of error of the measurements. (3) a test of ICD integrity was performed 3 days after MR scan. VF was induced, and the ICD sensed the VF properly and terminated the arrhythmia with a 20-J shock, unchanged from the implantation procedure in 2004; and (4) serum troponin was 0.02 ng/mL before and 0.00 ng/mL after the procedure, without any evidence of MRI-related myocardial damage.

The authors concluded that no evidence of adverse effects to the patients was noted during or after MRI, and that the imaging results indicated a recurrent astrocytoma. The patient was referred for chemotherapy for recurrent astrocytoma. The authors also recommended: "A complete ICD check is required before and immediately after MR scanning. Moreover, we strongly recommend performing an ICD device test, including induction of VF after the MR scan to ensure a fully competent ICD system. Additional testing, that is, an ICD follow-up six weeks after MR scanning, should be performed to assess potential late effects."

CMS Literature Search:

Our search was limited by the paucity of available clinical studies of any type (including case reports) describing either the benefits of MRI testing, or the risk of adverse effects of MR scanning in patients with PM or ICDs.

CMS staff performed an internal literature search to identify all published reports of clinical studies published between 01/01/2000 and 09/01/2010 containing terms identifying both "magnetic resonance imaging" and adverse events of PMs or ICDs. Reports of animal studies or reports on radiologic phantoms, as well as case series including less than 12 participants, were not included. [Please note that the scope of the internal technology assessment literature search conducted in connection with this PDM was broader than that undertaken for one aspect of the 2009 MRI-related NCD (CAG-00399R)]. The proposed DM posted December 1, 2010 indicated: "CMS performed a literature search on 5/18/2009 utilizing PubMed for search terms involving MRI and pacemakers. We also looked to see if there are any pacemakers or cardioverter-defibrillators approved by FDA as safe for use in an MRI environment. Our search failed to produce any evidence that any such devices exist at this time." Subsequently, however, on February 8, 2011, the FDA announced the approval of the first pacemaker for use during certain MRI exams. The FDA approval occurred after the close of the public comment period on the proposed decision memorandum, and occurred too late to be fully considered as part of this national coverage analysis.

Of the ten articles found in PubMED from this search, two had been submitted by the requester (Naehle et al., 2009 and Nazarian et al., 2006). The remaining eight articles found by CMS included three clinical studies that are unrelated to the topic of this decision memo. Based on PubMED abstracts, two of these (Kadish et al., 2009 and Schmidt 2007) used MRI to determine infarct size in patients who later had ICD implantation, while the third (DeWilde et al., 2008) used MRI to detect evidence of suspected right ventricular dysplasia/cardiomyopathy being evaluated for possible ICD implantation. CMS staff did not review the full text of these three articles because they were not relevant to either of the assessment questions (Q1 and Q2).

Six articles were obtained in full-text form by CMS staff and reviewed. These are listed below and summarized with other articles in the table in the following section.

Al-Sabagh, Christensen BE, Thoegersen AM, et al., "Safety of MRI in patients with pacemaker and implantable defibrillator." Ugeskr Laeger. 2010 Jun 7; 172(23):1740-4.

In this case series, the authors investigated the safety of MR scanning in 60 patients with implanted PMs (eight of whom were pacemaker dependent) and five patients with implanted ICDs. In this study, 46 patients were male and 19 patients were female. Implanted devices were produced by two manufacturers. All patients with a clinical indication for MR scanning underwent examination at a field strength of 1.5 Tesla. A safety protocol for all patients included: MR scan intensity and duration in each study patient was limited to a maximum energy absorption rate of 1.5 watts/kg and a total scan time of 30 minutes; and continuous patient monitoring with a physician, a bioanalyst, and resuscitation equipment present. Electrical characteristics of implanted devices were checked before and after the MR scan. Also, patients were encouraged to report any symptoms during MR scanning.

Study results showed that 73 MR scans were carried out in this group of 65 patients, with the most frequent scanned regions being the brain, spinal column, neck and lower extremities. In two cases, the MR scan was interrupted by clinical events. In one case, the patient's implanted pacemaker settings responded to a drop in battery voltage, which resulted in syncope and bradycardia. Removal of this patient from the MR scanner resulted in a return of prior pacemaker settings and clinical improvement. In the second case, the patient's ICD reset itself during the MR scan, inducing atrial fibrillation in the patient who went on to cardiac arrest. Other than these two situations, no patient reported abnormal or uncomfortable symptoms in connection with MR scanning. The authors found that the clinical questions for which MR scanning was indicated were answered for 70/73 (93%) of patients in the study. The authors noted that their study of devices from two manufacturers might be limited in generalizability to devices from other manufacturers, and that there was no data on long-term followup after MR scan. They also commented on the desirability of including greater numbers of ICD patients in future studies.

Burke PT, Ghanbari H, Alexander DB, et al. A protocol for patients with cardiovascular implantable devices undergoing magnetic resonance imaging (MRI): should defibrillation threshold testing be performed post-(MRI). J Interv Card Electrophysiol. 2010 Jun;28(1):59-66.

In this prospective case series, 38 patients with cardiovascular implantable electronic devices (CIED) underwent a total of 92 MRIs at 1.5 Tesla. Using a institution-developed safety protocol, 13 PM-dependent patients, ten ICD patients, four cardiac resynchronization therapy with defibrillator (CRT-D) patients, and eleven non-PM-dependent patients were scanned. The protocol used for each participant in the study included: an electrophysiologist was immediately available during each MR scan; except for PMD patients, each implantable device was switched before the scan to non-tracking, non-pacing mode; all ICD therapies were turned off; external PM, defibrillator, and resuscitation equipment were available on site; blood pressure and oximetry results were monitored closely during the MR scans; the MR staff were in verbal communication with the patients at all times during the MR scans; and post-MR scan interrogation and re-programming of CIEDs to pre-scan parameters. Age and gender information were not available for participants. Each participant's indication for MR scanning was reviewed to ensure that MRI would have a significant clinical impact over alternative imaging modalities.

Results: In the 92 MR scans performed, the most frequent site imaged was brain (n = 37), spine (different regions scanned, n = 44), and other regions (n=11) including lower extremities and pelvis. Mean MR scan duration was 26.1 minutes and did not statistically differ by region scanned or by implantable device type. All scans were successfully completed and were 'free of image quality limiting artifact attributed to the CIED.' No patient experienced spontaneous or device-induced arrhythmias. No unusual or noxious symptoms were reported by patients during the scans. Electromagnetic interference during the scan was interpreted as fast ventricular tachycardia or VF by nine of the 14 patients with ICD/CRT-Ds. Pacing thresholds and rate settings in CIEDs after MR scans were unchanged from pre-MR scan values. No electrical resets were observed. At three months' follow up, no changes in CIED electrical characteristics were observed compared to immediate post-MR values. The authors concluded that use of a safety protocol permitted safe, feasible and reproducible MR scanning of CIED patients. The authors also concluded that routine post-MR defibrillation response testing was not necessary.

Mollerus M, Albin G, Lipinski M, et al. Ectopy in patients with permanent pacemakers and implantable cardioverter-defibrillators undergoing an MR scan. Pacing Clin Electrophysiol. 2009 Jun;32(6):772-8.

This prospective observational study examined occurrences of ectopy (a cardiac conduction system defect in which myoelectrical signals for a heartbeat do not originate in the sinus node) during MR scanning in a series of patients with permanent PMs or ICDs who had clinical indications for MR imaging. Fifty-two patients underwent MR scans at 1.5 T without limitations on scan area or on peak specific absorption rate (SAR). Age and gender information on these patients were not provided in this report. Inclusion criteria included sinus rhythm on baseline assessment and implanted PM or ICD whose magnet mode could be disabled. Exclusion criteria included: (1) implantation of PM or ICD less than six weeks prior to the MR scan; (2) native ventricular rate less than 40 bpm; (3) presence of an epicardial pacing lead; or (4) having a device known to increase risk to MR scan exposure. Prior to each MR scan, patient's baseline cardiac rhythm (including ectopy) were assessed; baseline pacing thresholds, sensed amplitudes, and pacing impedances were measured; and device characteristics were programmed to disable magnet mode.

During each MR scan, patients were monitored by telemetry, oximetry, and plethysmography, including monitoring for ectopic beats by a cardiac electrophysiologist. Significant ectopy was defined as 20 or more ectopic beats during the entire scan. After each MR scan, the device was again interrogated and then re-programmed to pre-scan settings. During the study the 52 patients with 119 leads underwent 59 MR scans. Scans of the head (n=33) and truncal area (including thorax and lumbar spine areas) (n=27) were performed. As per protocol 29 scans were excluded from analysis because of pre-existing atrial fibrillation or flutter, baseline ectopy, or inability to disable magnet mode. Onset of atrial fibrillation during the scan was noted in one patient. Results of the study revealed the following: Seven of 52 patients had significant ectopy observed either by telemetry or by oximetry monitoring when MR artifact interfered with telemetry interpretation. Significant ectopy was found in five head scans, and two truncal scans. Significant ectopy was noted during T1 spin echo, T1 turbo spin echo, T2 turbo spin echo, fluid-attenuated inversion recovery and diffusion scans. The median peak SAR was 2.6 watts/kilogram, ranging from 1.3 to 3.2 W/kg. No significant association between peak SAR and presence of significant ectopy was noted. In five of seven patients with significant ectopy, the ectopic source was ventricular; in the other two, MR artifact made interpretation of the source of the ectopic beat impossible.

The authors concluded that a minority of patients with implanted pacemakers may have MRI-related ectopy. They suggested that in four of seven patients with significant ectopy during MR scans, timing of ectopic beats suggested that the pacemaker's noise-rejection behavior may result in asynchronous pacing due to excessive electromagnetic noise from the MR scanner.

Mollerus M, Albin G, Lipinski M, et al. Cardiac biomarkers in patients with permanent pacemakers and implantable cardioverter-defibrillators undergoing an MR scan. Pacing Clin Electrophysiol. 2008 Oct;31(10):1241-5.

This prospective observational study examined changes in serum troponin and myoglobin levels before and after MR scanning in a series of patients with permanent PMs or ICDs who had clinical indications for MRI. Thirty-seven patients underwent 40 MR scans at 1.5 T without limitations on scan area or on peak specific absorption rate (SAR). Age and gender information on these patients were not provided in this report. Inclusion criteria included sinus rhythm on baseline assessment and implanted PM or ICD whose magnet mode could be disabled. Exclusion criteria included: (1) implantation of PM or ICD less than six weeks prior to the MR scan; (2) native ventricular rate less than 40 bpm; (3) presence of an epicardial pacing lead; or (4) having a device known to increase risk to MR scan exposure. Prior to each MR scan, patient's baseline cardiac rhythm (including ectopy) were assessed; baseline pacing thresholds, sensed amplitudes, and pacing impedances were measured; and device characteristics were programmed to disable magnet mode.

During each MR scan, patients were monitored by telemetry, oximetry, and plethysmography, including monitoring for ectopic beats by a cardiac electrophysiologist. After each MR scan, the device was again interrogated and then re-programmed to pre-scan settings. Serum samples to measure cardiac troponin-I and myoglobin were obtained at baseline; immediately after MR scanning; and also 6-12 hours after MR scanning. Results of the study revealed no significant pre- to –post-MR scan changes in either troponin-I or myoglobin. Pacing capture thresholds also remained unchanged. No patient had an adverse clinical event related to the scan. The authors concluded that the absence of changes in cardiac biomarkers after MR scan indicated that local tissue effects of the scan (such as heat or edema, observed in other studies) were not sufficient to lead to significant myocardial necrosis. The authors suggest that factors other than SAR and anatomic scan area may affect MR scan-related myocardial injury.

Mollerus M, Albin G, Lipinski M, and Lucca J. Magnetic resonance imaging of pacemakers and implantable cardioverter-defibrillators without specific absorption rate restrictions. Europace 2010 July; 12(7): 947–951.

This prospective observational cohort study evaluated whether an increased peak specific absorption rate (SAR) (in units of absorbed energy per second per unit mass, i.e., watts/kilogram (W/kg)) was associated with the safety profile of patients with pacemakers or implantable cardioverter-defibrillators (ICDs) undergoing a medically necessary magnetic resonance imaging (MRI) scan. The study population included patients whose results had already been published (in Mollerus et al., 2008, and Mollerus et al., 2009, summarized above). Devices must have been in place for at least 6 weeks at the time of the scan and have a battery status that was beginning of life (BOL). Patients were excluded if they had a native ventricular rate of < 40 beats per minute, had an epicardial pacing lead, had a known or suspected fractured lead, had a generator with battery status that was at elective replacement indicator (ERI) or end of life (EOL), or had a device with known increased risk to exposure to an MRI scan. In this study, SAR was not limited but was allowed to vary between patients based on the standard peak SAR required for the type of scan performed. One-hundred and three patients with a total of 240 leads underwent a total of 127 scans of any body landmark using usual protocols with standard peak SAR settings for the scan. No patient was pacemaker dependent. Thresholds were obtained immediately before and after the scan.

For all scans, the median (25th and 75th percentiles) peak SAR was 2.5 (1.3, 3.2) W/kg whereas the median scan time was 1650 (1236, 2099) seconds. Pre- and post-scan pacing thresholds were unchanged [0.7 (0.5, 0.8) vs. 0.6 (0.5, 0.8) Volts at 0.5 ms, P = NS], though the sensed amplitudes [6.7 (2.9, 11.5) vs. 6.1 (2.9, 11.2) millivolts, P < 0.0001] and pacing impedances [500 (440, 609) vs. 491 (437, 593) ohms, P < 0.0001] both decreased significantly. One patient experienced the onset of atrial fibrillation during a scan. One pacemaker had a 'device reset' which required reprogramming. One ICD had its arrhythmia log erased during a scan. No significant changes in battery status were seen immediately following a scan. No significant study-related events were seen at the 3-month follow-up. The authors concluded that, based on this series of patient results, MRI scans may be performed safely in appropriately selected patients up to a peak SAR of 3.2 W/kg. Furthermore, peak SAR level poorly predicts the safety profile of patients with pacemakers or ICDS who are exposed to an MRI environment. The authors cautioned that the study was not sufficiently powered to detect low-frequency adverse events; and that the study's results should not be extended to pacemaker-dependent patients.

Additional note on Mollerus et al., 2010: the first author subsequently clarified (Europace 2010 Dec; 12(12): 1798 (e-published August 14, 2010)) that the term 'peak' as used in this study referred to "… the maximum value for a given sequence of scans for a specific patient session. For example, if scan session values ranged from 0.8 to 2.0 W/kg, then 2.0 W/kg was reported. The recorded SAR was from the console reading of the Siemens Symphony scanner, which reports SARs differently from other manufacturers."

Schmiedel A, Hackenbroch M, Yang A, et al. MRI of the brain in patients with cardiac pacemakers: experimental and clinical investigations at 1.5 T. Fortschr Roentgenstr 2005 May;177(5):731-44.

This study investigated the MRI-compatibility of PMs if the MR scan was limited to the brain. Pre- and post- MR scan evaluation of the PM was performed with additional safety precautions including continuous patient monitoring and device reprogramming prior to MR scanning. 63 MR scans of the brain were performed in 45 patients with implanted PMs and atrial and/or ventricular leads from multiple manufacturers. Safety steps included limitation of specific absorption rate (1.2 Watts/kg). After analyzing the data, the authors stated that all clinical examinations were completed with no complications, and no patients complained of any symptoms during the MR scans. All programmed PM settings were unchanged after MRI. No statistically significant changes were found in any pacemaker or lead electrical characteristics assessed, including: lead impedances and pacing capture thresholds. The authors noted that changes in pacing capture threshold were below the level of clinical significance. The authors acknowledged several limitations in this study, including limited generalizability to other brands of MR scanners. They concluded that with appropriate patient selection prior to MR testing and with safety precautions in place, pacemakers should no longer be regarded as an absolute contraindication for MR scanning of the brain at 1.5 T.

4. MEDCAC

A Medicare Evidence Development Coverage Advisory Committee (MEDCAC) meeting was not convened on this request.

5. Evidence-based guidelines

At www.guidelines.gov, the National Guideline Clearinghouse, a search for 'magnetic resonance imaging' provides more than 450 guidelines referring to MRI use in the diagnosis and management of a large variety of clinical situations. A large number of other guidelines are available through www.guidelines.gov covering MRI use in various oncologic, cardiovascular, neurodegenerative, traumatic and other diseases or conditions. In 12 guidelines, both 'MRI' and 'pacemaker' occur.

Recommendations from these guidelines generally contraindicate MRI use in patients with implanted PMs. Many of these guidelines are based not only on reviews of published literature, but also on consensus of experts.

An example of such a guideline was developed in the United Kingdom. The National Institute for Health and Clinical Excellence (NICE) 2008 guideline on MRI for diagnosis of patients with suspected stroke lists pacemakers among the contraindications to MRI use; however, the NICE recommendation is modified by its statement that " … the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summary of product characteristics of any drugs they are considering."

6. Professional Society Position Statements

In 2007, several professional societies suggested that the presence of an implanted PM or ICD should be considered as a relative contraindication[1] to MRI. The AHA, the North American Society for Cardiac Imaging, and the Society for Cardiovascular Magnetic Resonance endorsed this document (Levine et al., 2007).

The ACR guidelines on MRI safety (Kanal et al., 2007) noted that adverse effects of MR scans on implanted cardiac devices can include " … [u]nexpected programming changes, inhibition of pacemaker output, failure to pace, transient asynchronous pacing, rapid cardiac pacing, the induction of VF, heating of the tissue adjacent to the pacing or ICD system, early battery depletion, and outright device failure requiring replacement may all occur during MRI of patients with pacemakers or ICDs. The ACR Blue Ribbon Panel on Magnetic Resonance Safety committee noted that multiple deaths have occurred under poorly and incompletely characterized circumstances when device patients underwent MRI. These deaths may have occurred as a result of pacemaker inhibition, failure to capture or device failure (resulting in prolonged asystole), and/or rapid cardiac pacing or asynchronous pacing (resulting in the initiation of ventricular tachycardia or fibrillation)." Nevertheless, the ACR panel suggested that "… It is recommended that **the presence of implanted cardiac pacemakers or implantable cardioverter defibrillators (ICDs) be considered a relative contraindication for MRI. MRI of patients with pacemakers and ICDs ('device patients') is *not* routine.** Should an MRI be considered, it should be done on a case-by-case and site-by-site basis, and only if the site is staffed with individuals with the appropriate radiology and cardiology knowledge and expertise on hand." (Note: Emphasis in bold font added by CMS.)

7. Expert Opinion

We did not receive expert opinions on the use of MRI in patients with implanted PMs or ICDs.

8. Public Comments

A. Initial Comment Period 6/28/2010- 7/28/10

During the initial public comment period, CMS received three public comments. One comment came from industry, one comment came from a public interest group and one comment came from an industry consultant. Two of the three commenters were non-supportive of the request to remove PM as a contraindication at Chapter 2, Section 220.2.C.1 in the NCD Manual and allow for the national coverage of PM or ICD in prospective clinical trials with IDE approval to assess the risk of PM and ICD use in the MRI environment, due to the fact that at the close of the initial public comment period, there was no PM or ICD FDA-approved for use in the MR environment.

B. Public Comment Period 12/1/2010- 12/31/2010

Five commenters wrote to CMS in response to our proposed decision. Multiple positions were presented, which will be discussed below. Comments came from a national association of health insurance plans, a medical society, medical technology companies, and a clinician.

Comment

One commenter expressed concern that there are no implanted ICDs or PMs approved by the FDA for use in MRI, nor is there an Investigation Device Exemption (IDE) for this use. The commenter believed that CMS should retain the current contraindication policy or patients may be placed at risk.

Response

As stated in the FDA status section of this NCA, the FDA recently announced the approval of the first pacemaker for use in the MRI environment under certain circumstances. Once the FDA releases more details surrounding this approval, we expect a formal request to re-open this decision. Moreover, we understand that FDA has also approved at least one device as an IDE. The recent FDA actions, however, do not answer the question of whether an MRI can be safely performed on patients with other legacy devices. The comments do not suggest that the added safety steps that would be included under the CED trial would be inadequate to protect patients. We believe that with these appropriate safeguards, patients will not be placed at significant risk. Thus, we are making one exception to our contraindication in this policy for those CED trials.

Comment

One commenter believed that coverage for MRI within a clinical study, after an IDE is granted does not comply with Medicare's current Clinical Trial Policy.

Response

Prior to the release of this decision, existing national non-coverage prevented payment under either the Clinical Trial Policy or the IDE regulation. Our proposal to create a limited exception to the contraindication policy to enable research using coverage with study participation is fully consistent with the clinical trial policy in §310.1. That NCD specifically allows CMS to use the NCD process to cover items or services in a clinical trial that meets the requirements defined in that NCD based on individualized assessment of the benefits, risks, and research potential. This policy is further described in the guidance document on CED (Retrieved on February 15, 2011 from: http://www.cms.gov/medicare-coverage-database/details/medicare-coverage-document-details.aspx?MCDId=8&McdName=National+Coverage+Determinations+with+Data+Collection+as+a+Condition+of+Coverage%3a+Coverage+with+Evidence+Development&mcdtypename=Guidance+Documents&MCDIndexType=1&bc=BAAIAAAAAAAA&). Thus, our decision is fully consistent with the clinical trial policy.

Comment

Several commenters stated that CMS should provide coverage for patients with cardiac devices that undergo MRI when it is performed as part of a registry that will monitor and record the risk of the procedure, as well as outcomes.

Response

While registries have methodologic limitations that may affect the conclusions that may be drawn from their results, we have not excluded the consideration of registries from coverage, to the extent that these may be registries that can comply with the requirement of this decision.

Comment

Two commenters stated that CMS should only be focused on the safety of using MRI in beneficiaries with implanted PMs or ICDs. They believe that MRI has already been proven to improve beneficiaries' health outcomes, and therefore, this decision should not require re-proving MRI's benefit.

Response

We agree with the comments that MRIs are very useful diagnostic tests for most patients. Our NCD focuses on a particular group of patients, those with implanted PMs or ICDs. As explained in the proposed decision, CMS believes that the specific increased risk to patients with implanted PMs or ICDs has not been sufficiently investigated to ascertain the causes, risk factors, and protective steps appropriate for such patients during MRI procedures. CMS includes such risks within its assessment of the health outcomes that accrue from the use of diagnostic technology. In the population for whom this NCD may be of greatest use, a careful review of the risks and benefits based on evidence from appropriately focused clinical studies seems prudent. With adequate safeguards provided in the CSP trials, we believe patients will be appropriately protected.

Comment

One commenter was concerned that adoption of our proposed decision would create logistical barriers for patients to receive MRIs, which would unfavorably impact patient care and outcomes.

Response

We remind the reader that the scope of this NCD is limited to the use of MRI for patients with implanted PMs or ICDs, which is currently noncovered nationally. Thus our provision of CED-dependent coverage removes a significant logistical barrier for those seeking Medicare coverage. In light of recent medical advances and the approval by the Food and Drug Administration, additional expansion may be considered in future national coverage determinations.

Comment

One commenter submitted additional references to assert a benefit of MRI in patients with ICDs and pacemakers.

Response

CMS reviewed three references (Executive Committee for the Asymptomatic Carotid Atherosclerosis Study 1995, Barnett et. al. 1998, and Hobson et. al. 1993) submitted by this commenter because they were not previously reviewed in our proposed decision.

All three references submitted by this commenter are clinical studies of carotid endarterectomy, not of implanted cardiac devices. MRI procedures are only mentioned in the articles as diagnostic tools to detect and/or confirm the presence of a major study endpoint: the presence of stroke. For that reason, CMS finds that they provide no persuasive evidence relevant to the topic, but includes them in the bibliography since we mention them here.

Comment

One commenter submitted ten references to support the consideration of registry-based clinical studies to determine MRI safety.

Response:

As mentioned in a prior response to a different public comment, we appreciate the commenter's interest in registry-based clinical studies of MRI safety, and will welcome specific design proposals for such studies.

CMS reviewed the ten references submitted by this commenter. Six of the ten (i.e., Faris and Shein 2006, Levine et al., 2007, Naehle et al., 2009, Nazarian et al., 2006, Mollerus et al., 2009, and Sommer et al., 2006) had been considered in the proposed decision memorandum either as articles for background information or as sources of clinical study information, and are listed in its bibliography.

Of the other four references in this public comment not present in our proposed decision memorandum, one reference (Gimbel 1995) is an abstract of a clinical study. CMS does not generally find sufficiently detailed information about primary clinical research in abstracts to include them as evidence in our coverage determinations.

The second of these other four references is a review article (Götte 2010), which in our view provides a helpful summary of current concerns about MRI in beneficiaries with implanted PMs and other devices, but does not represent original clinical research on this issue.

The third of these four references cites "Cardiac Pacing and Defibrillation: A Clinical Approach" by Hayes et al. (2000), a textbook of electrophysiology that, while valuable, is not a source of original clinical research relevant to this issue.

The last of the four references (Mollerus et al., 2010) provided in the public comment describes a clinical research study which we believe may be relevant to this topic. CMS thanks the commenter for this reference, which has been reviewed as a full-text article, summarized and added to this section (see above), included in the bibliography (below) and included as a tabular summary in the Table of Evidence (Appendix B below).

VIII. CMS Analysis

NCDs are determinations by the Secretary with respect to whether or not a particular item or service is covered nationally by Medicare (§1862(l) of the Act). In order to be covered by Medicare, an item or service must fall within one or more benefit categories contained within Part A or Part B, and must not be otherwise excluded from coverage. Moreover, with limited exceptions, items or services must be "reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member." See §1862(a) (1) (A) of the Act.

We begin generally with an explanation of the basis for Medicare decisions about diagnostic tests such as MRI. The Medicare regulations at 42 CFR 410.32(a) state in part, "…diagnostic tests must be ordered by the physician who is treating the beneficiary, that is, the physician who furnishes a consultation or treats a beneficiary for a specific medical problem and who uses the results in the management of the beneficiary's specific medical problem." Thus, in making or modifying an NCD on MRI, we look for evidence demonstrating how the treating physician uses the result of an MRI study to manage the further diagnostic or treatment strategy in Medicare beneficiaries with implanted PMs or ICDs. We believe that evidence of improved health outcomes is more persuasive than evidence of test characteristics.

We considered the evidence in the hierarchical framework of Fryback and Thornbury (1991) where Level 2 addresses diagnostic accuracy, sensitivity, and specificity of the test; Level 3 focuses on whether the information produces change in the physician's diagnostic thinking; Level 4 concerns the effect on the patient management plan and Level 5 measures the effect of the diagnostic information on patient outcomes.

In evaluating diagnostic tests, Mol and colleagues (2003) reported: "Whether or not patients are better off from undergoing a diagnostic test will depend on how test information is used to guide subsequent decisions on starting, stopping, or modifying treatment. Consequently, the practical value of a diagnostic test can only be assessed by taking into account subsequent health outcomes." When a proven, well established association or pathway is available, outcomes may also be considered. For example, if a particular diagnostic test result can be shown to change patient management and other evidence has demonstrated that those patient management changes improve health outcomes, then those separate sources of evidence may be sufficient to demonstrate positive health outcomes from the diagnostic test.

As a diagnostic test, an MRI study would not be expected to directly change health outcomes absent adverse effects of the MR scan itself. Rather, it would affect health outcomes through changes in disease management brought about by physician actions taken in response to test results. Such actions may include decisions to treat or withhold treatment, to choose one treatment modality over another, or to choose a different dose or duration of the same treatment. To some extent the usefulness of a test result is constrained by the available management alternatives. Ideally we would see evidence that the use of MRI changes outcomes for Medicare beneficiaries with implanted PMs or ICDs, or at least leads treating physicians to change their diagnostic or treatment strategies in such a way that better outcomes are achieved.

In addition, CMS generally focuses on evidence that includes patients who are 65 years of age or older. The typical Medicare beneficiary is 65 years of age or older; however, a relatively small percentage of beneficiaries may be younger than 65 year old due to Medicare entitlement based on other factors such as end stage renal disease or disability. CMS favors evidence from studies in which the population reflects the affected Medicare beneficiary population.

As the clinical studies submitted by the requester and found by CMS in a literature search were analyzed, CMS found for a number of reasons that these studies were generally poor sources of evidence about the key question for this NCA and thus we must assign them lower evidentiary weight. Ideally, we would like to see results of peer -reviewed studies, published in English, comparing the effectiveness of MRI in patients with PMs or ICDs for patient-centered outcomes (e.g., diagnostic accuracy), based on multi-center randomized controlled clinical trials involving, in each arm of the study, 30 or more patients comparable to the Medicare population. We would have liked to find published articles of such studies in historically underserved patient populations. Studies used in this analysis can be found in the evidence table in Appendix B. Major concerns about evidence quality included:

1. No studies were designed as prospective controlled trials. In the hierarchy of evidence, prospective (rather than retrospective) studies ensure a more thorough and systematical assessment of factors related to outcomes because prospective studies are less prone to bias, as well as the effects of confounding;
2. Most studies were case series, which have lower evidentiary validity.
3. Two case series were wholly or partially based on retrospective data collection, which may increase the potential for bias (Martin 2004 and Naehle 2009B). Prospective (rather than retrospective) studies ensure a more thorough and systematical assessment of factors related to outcomes.
4. The small size of most of the studies (N < 20 in five of twelve studies: DelOjo 2005, Gimbel 1996, Gimbel 2005, Gimbel 2005B, and Naehle 2006) limits statistical power of study to detect low-frequency adverse events or to precisely estimate any effects detected during study. Statistical assumptions were violated. For studies with less than 30 participants the authors did not provide information about whether or not the data was normally distributed. To make comparable comparisons the data should have been transformed to use t-test statistic, or the Sign test should have been used if the data was not normally distributed.
5. Several studies involved devices (or in one case, a scanner) from only one manufacturer, which limits generalizability (Del Ojo 2005, Gimbel 2005, Sommer 2006, and Mollerus 2010).
6. Several studies raised methodological questions about accuracy or precision of study measurements (for example, lack of precision in voltage measurement, or indicated uncertainty about the relationship of the specific absorption rate (SAR) as indicated by one type of scanner to the SAR indicated by other types of scanners) and about statistical techniques (see following table for examples).
7. One study indicated that a pre- to post-MR scan change in troponin-I levels was statistically significant, but did not comment on its clinical significance in evaluating myocardial damage.
8. In the Gimbel 2005 study, the operational definition of pacemaker dependence was different from other authors' definition of the term. This could lead to study heterogeneity due to misclassification.

9. One of the articles submitted by the requestor was a single case study (Naehle CP et al 2006). In general, case studies do not have the evidentiary weight as other research designs (e.g., randomized clinical trials, cohort studies, etc.). But this study is unique among the 16 studies reviewed, because it not only assessed whether PMs and ICDs could be performed safely in an MRI environment, but also the results of the study were used in the medical management of the patient. None of the fifteen other studies considered whether or how the results of the MRI were used to improve patient outcomes or even to make patient care decisions.

CMS is concerned about disparities in healthcare in the Medicare population, and when performing this assessment of the literature, there was little information addressing age, gender, race/ethnicity; socioeconomic status; or sexual orientation of study participants. Because of this, these studies provide only weak evidence on which to base conclusions that CMS considers generalizable to Medicare beneficiaries.

CMS also wants to make sure not only that diagnostic interventions are associated with minimal adverse effects on patients, but also that results of these diagnostic tests lead to treatment decisions that improve patient outcomes. Studies in the medical literature have documented some untoward events associated with MRI use in patients with PMs and ICDs. In particular, studies reviewed for this decision memorandum that document potentially serious adverse events occurring to patients with implanted devices during MR scanning include Gimbel 2005B, Martin 2004, Mollerus 2009, Mollerus 2010, Nazarian 2006, and Al-Sabagh 2010.

Finally, most of these studies, while evaluating the safe use of MRIs in patients with PMs and ICDs, have failed to show that the results have been used to improve patient outcomes. As noted above and in Table 1 (which summarizes all studies), only the Naehle 2006 study comments on patient care management decisions as a result of this diagnostic test.

Table 1: Summary of studies and findings

Authors (year)	N:	Demographic Information:	Key Findings re: Adverse Events, Image Quality or Patient Outcomes or Care Decisions:
Del Ojo 2005	13	Yes	Not mentioned
Gimbel 1996	5	No	In one case, artifact from the PM 'compromised' the MRI image for evaluating the patient's cardiac valve.
Gimbel 2005	10	No	All MR imaging studies produced diagnostic studies for the clinical question presented by the referring physicians

Authors (year)	N:	Demographic Information:	Key Findings re: Adverse Events, Image Quality or Patient Outcomes or Care Decisions:
Gimbel 2005B	7	No	One participant experienced "painless involuntary muscle reaction like twitching several times" of his left upper pectoral region and upper extremity during the MRI. This sensation stopped as the MR scan ended, and did not recur. This patient's ICD underwent an electrical reset or "Power On Reset" (POR) during MRI.
Martin 2004	54	No	Two patients reported symptoms; vibration (n=1) and palpitations (n=1) coinciding "with inhibition of the pacing lead." EM interference during the MR scan was noted to resemble arrhythmias (VF). In the Discussion section, the authors mention that even though some 'significant' PM threshold changes were observed, they had no clinical importance.
Naehle 2006	1	33 y.o. M	In this patient with history of astrocytoma, imaging results indicated recurrence; patient was referred for chemotherapy for recurrence of disease.
Naehle 2009B	47	No	Although the authors mention that the changes in battery voltage were approximately 0.001 V per MR scan, they mention elsewhere in the article that the measurement error was far larger (30% or 0.1 V). In addition, their explanation of the use of regression analysis to detect trends in certain PM parameters did not explain the basis for statistical analysis with such imprecise data.
Naehle 2009	18	61.8 (35-84) years	No adverse effect or impact on outcomes was mentioned
Nazarian 2006	55	No	In ten of 31 patients whose permanent PMs lacked magnet-mode programming capability, reed switch activation by the static magnetic field of MRI led to transient asynchronous pacing at the device-specific rate (85 ppm). This effect ceased on patient positioning in the magnet bore. Also, answers to clinical questions were successfully determined in 27 of 29 (93%) thoracic MR scans, and in all 39 (100%) non-thoracic MR scans.
Sommer 2006	82	Yes	

Authors (year)	N:	Demographic Information:	Key Findings re: Adverse Events, Image Quality or Patient Outcomes or Care Decisions:
			No adverse events were found. No impact on outcomes was mentioned.
Al-Sabagh (2010)	65	M:F::46:19	Two MR scans interrupted due to clinical adverse events related to the implanted device. One MR image (of thoracic spine) with PM artifact.
Burke 2010	38	No	All scans were successfully completed. MR images were 'free of image quality limiting artifact' attributed to the implanted device.
Mollerus 2009	52	No	Onset of atrial fibrillation during the scan was noted in one patient. Seven of 52 patients had significant ectopy observed either by telemetry or by oximetry monitoring when MR artifact interfered with telemetry interpretation.
Mollerus 2008	37	No	No significant pre- to post-MR scan changes were seen in troponin-I or myoglobin values. No patient had an adverse event related to the scan.
Mollerus 2010	103	No	One pacemaker had a 'device reset' which required reprogramming. One ICD had its arrhythmia log erased during a scan. In one patient, also noted (above) in Mollerus 2009, the onset of atrial fibrillation was noted. No significant changes in battery status were seen immediately following a scan. No significant study-related events were seen at the 3-month follow-up.
Schmiedel (2005)	45	No	In one case, artifact from the PM 'compromised' the MRI image for evaluating the patient's cardiac valve.

Evidence of improvement of patient outcomes (or surrogate indicators of improved clinical decision making) is rarely addressed in these studies. In one, the authors mention without providing data that MR images in patients with implanted cardiac devices answered 100% of clinical diagnostic questions concerning non-thoracic regions, and 93% of questions involving thoracic regions (Nazarian 2006). However, comments about artifacts in MR images due to implanted PMs or ICDs were rare in the clinical studies reviewed by CMS (Gimbel 1996, Al-Sabagh 2010, and Schmiedel 2005).

But many, including professional organizations as well the professional guidelines created by these organizations, consider MR scanning to be contraindicated or "relatively contraindicated" for patients with PMs and ICDs. While plausible, the guidelines provide little in the way of evidence-based studies bolstering their position. We were not able to find any guidelines which indicate the use of MRIs in patients with ICDs.

CMS finds that two major conclusions drawn by the requester are persuasive. First, there may be significant benefit to Medicare beneficiaries with implanted PMs and ICDs who require the use of MRI, and there is need for additional research on providing such diagnostic imaging services with improved safety. Secondly, a patient with a permanent pacemaker or ICD will have an estimated 50-75% chance of requiring an MRI during the lifetime of the implanted device. Improved access to MRI for Medicare PM/ICDs beneficiaries could improve health outcomes via changes in patient management. We are also encouraged that MRI safety has been addressed in some detail by appropriate professional societies (as in Kanal 2007, Levine 2007).

However, while understanding the requester's concern, CMS believes that prudence mandates that any prospective clinical study will not only be designed to answer questions of clinical utility (i.e., improvement of patient health outcomes or at least effect on clinical decision-making), but also include precautions to minimize adverse effects of MRI on trial participants.

In summary, we agree with the requestor that the use of MRI in patients with PMs and ICDs, a clinically important question for the Medicare beneficiary population, should be addressed by additional research. We believe that the decision provides clear guidance to design effective studies of MRI utility in a systematic and scientifically rigorous manner while assuring patient safeguards are in place, as discussed further below.

However, CMS believes that the available evidence is insufficient to determine that MRI in patients with implanted devices is reasonable and necessary under section 1862(a)(1)(A) of the Act.

Coverage with Evidence Development (CED)
As explained in the CED Guidance Document of July 2006, §1862(a)(1)(E), provides, in pertinent part, for Medicare coverage for items and services in some circumstances.

(a) Notwithstanding any other provision of this title, no payment may be made under part A or part B for any expenses incurred for items or services—
. . .
(E) in the case of research conducted pursuant to section 1142, which is not reasonable and necessary to carry out the purposes of that section[.]
. . .

Section 1142 describes the authority of the AHRQ. Under section 1142, research may be conducted on the outcomes, effectiveness, and appropriateness of health care services and procedures to identify the manner in which diseases, disorders, and other health conditions can be prevented, diagnosed, treated, and managed clinically.

Under the authority of § 1862(a)(1)(E), Medicare may cover under coverage with evidence development (CED) certain items or services for which the evidence is not adequate to support coverage under §1862(a)(1)(A), and where additional data gathered in the context of clinical care would further clarify the impact of these items and services on the health of Medicare beneficiaries. Further guidance on CED can be found at http://www.cms.gov/medicare-coverage-database/details/medicare-coverage-document-details.aspx?MCDId=8&McdName=National+Coverage+Determinations+with+Data+Collection+as+a+Condition+of+Coverage%3a+Coverage+with+Evidence+Development&mcdtypename=Guidance+Documents&MCDIndexType=1&bc=BAAIAAAAAAAA& . CSP allows CMS to determine that an item or service is only reasonable and necessary when it is provided within a research setting where there are added safety, patient protections, monitoring, and clinical expertise.

For some items or services, CMS may determine that the evidence is preliminary and not reasonable and necessary for Medicare coverage under section 1862(a)(1)(A), but, if the following criteria are met, CED might be appropriate:

- The evidence includes assurance of basic safety;
- The item or service has a high potential to provide significant benefit to Medicare beneficiaries; and
- There are significant barriers to conducting clinical trials.

Regarding three criteria in view of the current request for modification of national contraindications to Medicare coverage for MRI in PM/ICD beneficiaries:

1. Both MRI and implantable PMs and ICDs have been in clinical use for years. Physicians are generally comfortable with these technologies in routine clinical situations. The degree to which these technologies have been adopted for clinical care is reflected not only in professional guidelines concerning appropriateness and safety, but also in Medicare coverage determinations for their use. (For examples, see Levine et al., 2007; and separately the NCDs on MRIs, PMs, and ICDs).
2. The importance of MRI as the sole available diagnostic imaging modality for certain types of studies (e.g., those of the central nervous system) indicates that MRI in Medicare beneficiaries with implanted PMs or ICDs could provide significant benefits for their care (in comparison to CT, for example). The requester's letter cites the large numbers of Medicare beneficiaries with implanted PM/ICDs who will develop medical indications for MRI, e.g., the need for brain MRI for staging of malignancy.
3. Current NCD language on contraindications prevents Medicare coverage for MRI in patients with these implanted devices, even for those involved in clinical studies of devices designed for safe and effective performance in the MR environment. Absent the requested coverage change in this NCA, participation in such studies of MRI benefits to health outcomes would not be available to PM/ICD beneficiaries who are unable to surmount the financial barriers for MRI.

There are some conditions attached to the types of clinical studies which would qualify for reimbursement for MRI. In particular, such a study must be designed to produce evidence to help assess whether the item or service should be covered by Medicare under §1862(a)(1)(A). Payment for the items and services provided in the study will be restricted to the Medicare qualified patients involved as human subjects in the study. These research studies will be rigorously designed and include in their protocols additional protections and safety measures for beneficiaries. In addition, the clinical study must be reviewed and approved by Medicare to assure its compliance with the AHRQ clinical study criteria including items a) – m), listed in section I of this decision memorandum.

Medicare beneficiaries with PMs and ICDs are already at an increased risk of medical complications due to their underlying condition. Thus we believe that a decision to allow this population to undergo additional diagnostic testing using MRIs is not inconsequential clinically, and must be tempered with an expectation of clinical benefit. As noted earlier there is the potential for providing significant benefit to this group. We believe that the current evidence indicates that MRI as a diagnostic tool to patients with PMs and ICDs is promising, especially since other alternative diagnostic tools (e.g., CT) may not be as accurate, and may not aid clinicians in making decisions which may be used in the management of those patients. Because of the limited diagnostic options for Medicare beneficiaries with PMs and ICDs, we have good reason to believe that access to MRIs under CED/CSP will be of substantial benefit to this population and would help to determine if this modality is effective for this group.

Summary

Based on the above, we believe that the evidence is promising although not yet convincing that MRI will improve patient health outcomes if certain safeguards are in place to ensure that exposure of the device to an MRI environment adversely affects neither the interpretation of the MRI result nor the proper functioning of the implanted device itself. In addition, we believe the MagnaSafe registry, which is being conducted by Dr. Robert Russo appears to meet the CED criteria outlined in this decision. Dr. Russo's registry is a prospective multicenter study designed to determine the risk of performing non-thoracic 1.5 MRI scanning for patients with implanted pacemakers and implantable cardioverter-defibrillators. This study has included a number of measures to ensure safety to the Medicare beneficiaries. We will also consider additional studies that meet the requirements set forth in this decision.

IX. Final Decision

The Centers for Medicare & Medicaid Services (CMS) determines that the evidence is not adequate to conclude that the use of magnetic resonance imaging (MRI) improves health outcomes for Medicare beneficiaries with implanted permanent pacemakers (PMs) or implantable cardioverter defibrillators (ICDs), and thus we determine that it is not reasonable and necessary under §1862(a)(1)(A) of the Social Security Act (the Act). Therefore, subject to one exception, we will to retain the current general contraindications at Chapter 1, Section 220.2.C.1 in the NCD Manual.

CMS believes that the evidence is promising although not yet convincing that MRI will improve patient health outcomes if certain safeguards are in place to ensure that the exposure of the device to an MRI environment adversely affects neither the interpretation of the MRI result nor the proper functioning of the implanted device itself. We believe that specific precautions (as listed below) could maximize benefits of MRI exposure for beneficiaries enrolled in clinical studies designed to assess the utility and safety of MRI exposure. Therefore, CMS determines that MRI will be covered by Medicare when studied in a clinical study under section 1862(a)(1)(E) (consistent with section 1142 of the Act) if the study meets the criteria in the three paragraphs below.

The approved prospective clinical study must, with appropriate methodology, address one or more aspects of the following questions:

1. Do results of MRI in PM/ICD beneficiaries with implanted cardiac devices affect physician decision making related to:
    a. Clinical management strategy (e.g., in oncology, toward palliative or curative care);
    b. Planning of treatment interventions; or
    c. Prevention of unneeded diagnostic studies or interventions, or preventable exposures?
2. Do results of MRI in PM/ICD beneficiaries with implanted cardiac devices affect patient outcomes related to:
    a. Survival;
    b. Quality of life;
    c. Adverse events during and after MR scanning?

In addition, the prospective clinical study of MRI must include safety criteria for all participants. Such required safety measures for such studies, as further explained in guidance documents from professional societies (e.g., Kanal et al., 2007; Levine et al., 2007), must include but are not limited to:

1. MRI should be done on a case-by-case and site-by-site basis.
2. MRI scan sequences, field intensity, and field(s) of exposure should be selected to minimize risk to the patient while gaining needed diagnostic information for diagnosis or for managing therapy.

3. MRI scanning should be done only if the site is staffed with individuals with the appropriate radiology and cardiology knowledge and expertise on hand.
4. Implanted device patients who are candidates for recruitment for an MRI clinical study should be advised that life-threatening arrhythmias might occur during MRI and serious device malfunction might occur, requiring replacement of the device.
5. Radiology and cardiology personnel and a fully stocked crash cart be readily available throughout the procedure in case a significant arrhythmia develops during the examination that does not terminate with the cessation of the MR study. The cardiologist should be familiar with the patient's arrhythmia history and the implanted device. A programmer that can be used to adjust the device as necessary should be readily available.
6. All such patients should be actively monitored for cardiac and respiratory function throughout the examination. At a minimum, ECG and pulse oximetry should be used. Visual and verbal contact with the patient must be maintained throughout the MRI scan. The patient should be instructed to alert the MRI staff on hand to any unusual sensations, pains, or to any problems.
7. At the conclusion of the examination, the cardiologist should examine the device to confirm that the function is consistent with its preexamination state.
8. Follow-up should include a check of the patient's device at a time remote (1–6 weeks) after the scan to confirm appropriate function.
9. If the implanted device manufacturer has indicated additional safety precautions appropriate for safe MRI performance, these must be included in the study protocol.

The clinical study must adhere to the following standards of scientific integrity and relevance to the Medicare population:

a. The principal purpose of the research study is to test whether a particular intervention potentially improves the participants' health outcomes.
b. The research study is well supported by available scientific and medical information or it is intended to clarify or establish the health outcomes of interventions already in common clinical use.
c. The research study does not unjustifiably duplicate existing studies.
d. The research study design is appropriate to answer the research question being asked in the study.
e. The research study is sponsored by an organization or individual capable of executing the proposed study successfully.
f. The research study is in compliance with all applicable Federal regulations concerning the protection of human subjects found at 45 CFR Part 46. If a study is regulated by the Food and Drug Administration (FDA), it must be in compliance with 21 CFR Parts 50 and 56.
g. All aspects of the research study are conducted according to appropriate standards of scientific integrity (see http://www.icmje.org).
h. The research study has a written protocol that clearly addresses, or incorporates by reference, the standards listed here as Medicare requirements for CED coverage.
i. The clinical research study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Trials of all medical technologies measuring therapeutic outcomes as one of the objectives meet this standard only if the disease or condition being studied is life threatening as defined in 21 CFR § 312.81(a) and the patient has no other viable treatment options.
j. The clinical research study is registered on the ClinicalTrials.gov website by the principal sponsor/investigator prior to the enrollment of the first study subject.
k. The research study protocol specifies the method and timing of public release of all prespecified outcomes to be measured including release of outcomes if outcomes are negative or study is terminated early. The results must be made public within 24 months of the end of data collection. If a report is planned to be published in a peer reviewed journal, then that initial release may be an abstract that meets the requirements of the International Committee of Medical Journal Editors (http://www.icmje.org). However a full report of the outcomes must be made public no later than three (3) years after the end of data collection.
l. The research study protocol must explicitly discuss subpopulations affected by the treatment under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion criteria effect enrollment of these populations, and a plan for the retention and reporting of said populations on the trial. If the inclusion and exclusion criteria are expected to have a negative effect on the recruitment or retention of underrepresented populations, the protocol must discuss why these criteria are necessary.

m. The research study protocol explicitly discusses how the results are or are not expected to be generalizable to the Medicare population to infer whether Medicare patients may benefit from the intervention. Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability or Medicaid eligibility.

Consistent with section 1142 of the Act, the Agency for Healthcare Research and Quality (AHRQ) supports clinical research studies that CMS determines meet the above-listed standards and address the above-listed research questions.

APPENDIX A

General Methodological Principles of Study Design

(Section VI of the Decision Memorandum)

When making NCDs, CMS evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service is reasonable and necessary. The overall objective for the critical appraisal of the evidence is to determine to what degree we are confident that: 1) the specific assessment questions can be answered conclusively; and 2) the intervention will improve health outcomes for patients.

We divide the assessment of clinical evidence into three stages: 1) the quality of the individual studies; 2) the generalizability of findings from individual studies to the Medicare population; and 3) overarching conclusions that can be drawn from the body of the evidence on the direction and magnitude of the intervention's potential risks and benefits.

The methodological principles described below represent a broad discussion of the issues we consider when reviewing clinical evidence. However, it should be noted that each coverage determination has its unique methodological aspects.

Assessing Individual Studies

Methodologists have developed criteria to determine weaknesses and strengths of clinical research. Strength of evidence generally refers to: 1) the scientific validity underlying study findings regarding causal relationships between health care interventions and health outcomes; and 2) the reduction of bias. In general, some of the methodological attributes associated with stronger evidence include those listed below:

- Use of randomization (allocation of patients to either intervention or control group) in order to minimize bias.
- Use of contemporaneous control groups (rather than historical controls) in order to ensure comparability between the intervention and control groups.
- Prospective (rather than retrospective) studies to ensure a more thorough and systematical assessment of factors related to outcomes.
- Larger sample sizes in studies to demonstrate both statistically significant as well as clinically significant outcomes that can be extrapolated to the Medicare population. Sample size should be large enough to make chance an unlikely explanation for what was found.
- Masking (blinding) to ensure patients and investigators do not know to which group patients were assigned (intervention or control). This is important especially in subjective outcomes, such as pain or quality of life, where enthusiasm and psychological factors may lead to an improved perceived outcome by either the patient or assessor.

Regardless of whether the design of a study is a randomized controlled trial, a non-randomized controlled trial, a cohort study or a case-control study, the primary criterion for methodological strength or quality is the extent to which differences between intervention and control groups can be attributed to the intervention studied. This is known as internal validity. Various types of bias can undermine internal validity. These include:

- Different characteristics between patients participating and those theoretically eligible for study but not participating (selection bias).
- Co-interventions or provision of care apart from the intervention under evaluation (performance bias).
- Differential assessment of outcome (detection bias).
- Occurrence and reporting of patients who do not complete the study (attrition bias).

In principle, rankings of research design have been based on the ability of each study design category to minimize these biases. A randomized controlled trial minimizes systematic bias (in theory) by selecting a sample of participants from a particular population and allocating them randomly to the intervention and control groups. Thus, in general, randomized controlled studies have been typically assigned the greatest strength, followed by non-randomized clinical trials and controlled observational studies. The design, conduct and analysis of trials are important factors as well. For example, a well designed and conducted observational study with a large sample size may provide stronger evidence than a poorly designed and conducted randomized controlled trial with a small sample size. The following is a representative list of study designs (some of which have alternative names) ranked from most to least methodologically rigorous in their potential ability to minimize systematic bias:

Randomized controlled trials
Non-randomized controlled trials
Prospective cohort studies
Retrospective case control studies
Cross-sectional studies
Surveillance studies (e.g., using registries or surveys)
Consecutive case series
Single case reports

When there are merely associations but not causal relationships between a study's variables and outcomes, it is important not to draw causal inferences. Confounding refers to independent variables that systematically vary with the causal variable. This distorts measurement of the outcome of interest because its effect size is mixed with the effects of other extraneous factors. For observational, and in some cases randomized controlled trials, the method in which confounding factors are handled (either through stratification or appropriate statistical modeling) are of particular concern. For example, in order to interpret and generalize conclusions to our population of Medicare patients, it may be necessary for studies to match or stratify their intervention and control groups by patient age or co-morbidities.

Methodological strength is, therefore, a multidimensional concept that relates to the design, implementation and analysis of a clinical study. In addition, thorough documentation of the conduct of the research, particularly study selection criteria, rate of attrition and process for data collection, is essential for CMS to adequately assess and consider the evidence.

Generalizability of Clinical Evidence to the Medicare Population

The applicability of the results of a study to other populations, settings, treatment regimens and outcomes assessed is known as external validity. Even well-designed and well-conducted trials may not supply the evidence needed if the results of a study are not applicable to the Medicare population. Evidence that provides accurate information about a population or setting not well represented in the Medicare program would be considered but would suffer from limited generalizability.

The extent to which the results of a trial are applicable to other circumstances is often a matter of judgment that depends on specific study characteristics, primarily the patient population studied (age, sex, severity of disease and presence of co-morbidities) and the care setting (primary to tertiary level of care, as well as the experience and specialization of the care provider). Additional relevant variables are treatment regimens (dosage, timing and route of administration), co-interventions or concomitant therapies, and type of outcome and length of follow -up.

The level of care and the experience of the providers in the study are other crucial elements in assessing a study's external validity. Trial participants in an academic medical center may receive more or different attention than is typically available in non-tertiary settings. For example, an investigator's lengthy and detailed explanations of the potential benefits of the intervention and/or the use of new equipment provided to the academic center by the study sponsor may raise doubts about the applicability of study findings to community practice.

Given the evidence available in the research literature, some degree of generalization about an intervention's potential benefits and harms is invariably required in making coverage determinations for the Medicare population. Conditions that assist us in making reasonable generalizations are biologic plausibility, similarities between the populations studied and Medicare patients (age, sex, ethnicity and clinical presentation) and similarities of the intervention studied to those that would be routinely available in community practice.

A study's selected outcomes are an important consideration in generalizing available clinical evidence to Medicare coverage determinations. One of the goals of our determination process is to assess health outcomes. These outcomes include resultant risks and benefits such as increased or decreased morbidity and mortality. In order to make this determination, it is often necessary to evaluate whether the strength of the evidence is adequate to draw conclusions about the direction and magnitude of each individual outcome relevant to the intervention under study. In addition, it is important that an intervention's benefits are clinically significant and durable, rather than marginal or short-lived. Generally, an intervention is not reasonable and necessary if its risks outweigh its benefits.

If key health outcomes have not been studied or the direction of clinical effect is inconclusive, we may also evaluate the strength and adequacy of indirect evidence linking intermediate or surrogate outcomes to our outcomes of interest.

Assessing the Relative Magnitude of Risks and Benefits

Generally, an intervention is not reasonable and necessary if its risks outweigh its benefits. Health outcomes are one of several considerations in determining whether an item or service is reasonable and necessary. CMS places greater emphasis on health outcomes actually experienced by patients, such as quality of life, functional status, duration of disability, morbidity and mortality, and less emphasis on outcomes that patients do not directly experience, such as intermediate outcomes, surrogate outcomes, and laboratory or radiographic responses. The direction, magnitude, and consistency of the risks and benefits across studies are also important considerations. Based on the analysis of the strength of the evidence, CMS assesses the relative magnitude of an intervention or technology's benefits and risk of harm to Medicare beneficiaries.

APPENDIX B
Evidence Tables

Tables 1-10: Evidence from articles suggested by requester

Tables 11-16: Evidence from CMS internal literature search

Evidence Table: (1 /16): Del Ojo et al., 2005

Publication	Design and Population	Intervention	Result and Conclusions:	Limitations
Authors: Del Ojo JL, Moya F, Villalba J, Sanz O, Pavo'N R, Garcia D, and Pastor L Objectives: (1) reassess risks of performing an MR scan in PM patients, (2) compare pacing functions before and after the exposure to MRI, and	Study Design: Prospective case series Population Studied: 13 participants included 10 males and 3 females. Their ages ranged from 59-79 years (median of 71 years). Duration of study – March 1999 to December 2001 Inclusion/Exclusion Criteria:	- Pre-MR assessment - Thoracic MR imaging at 2.0 T, with additional MR studies as required for head (3/13); cervical spine (2/13); neck (2/13); lumbar spine (1/13); with no additional studies in (5/13) - During MR scanning, - - Stimulation and sensing polarity was programmed to bipolar. - - The sensor, magnet, and AutoCapture™ functions were programmed OFF.	- PM Inhibition, asynchronous pacing, or inappropriately rapid pacing was not observed. - No patient reported discomfort, heat, or motion sensation at the PM implant site. - There were no significant differences in the sensing, stimulation, AutoCapture™ threshold, and lead impedance measurements before and after MRI. Author's conclusion: The results of this study suggest that performing 2.0 T-MR scans in patients with Affinity ™ DR model 5330 PM connected to a Tendril ™ model 1388 lead is safe.	Limitations noted by CMS: - Study is small (N=13). - Study results are limited to patients with a single model of leads and PM. Generalizability of findings to other implantable device types may be limited. (The expression of the author's conclusions suggests that they were aware of this limitation.)

Publication	Design and Population	Intervention	Result and Conclusions:	Limitations
(3) monitor the development of possible adverse effects. Title: "Is MRI Safe in Cardiac PM Recipients?" Citation: Pacing Clin Electrophysiol. 2005 Apr; 28: 274–8.	- Inclusion: patients with one type of PM and an indication for MR scan. - Exclusion: not described. Other baseline factors: - Indications for PM: sinus node disease in 7/13; for AV block: 6/13 (2/6 paroxysmal) - Type(s) of implanted devices: Affinity ™ DR model 5330 PMs (St. Jude Medical) connected to a Tendril ™ model 1388 leads (St. Jude Medical). - Pre-MRI patient status: All patients displayed a stable spontaneous rhythm at the time of the MR scan and were not considered to be PM-dependent.	- - Other functions, including Automatic Mode Switch, were allowed to remain enabled if originally enabled in the device. - Post-MR assessment of PM function; interviews with patient after MR scan.		- Followup of PM function in these patients was limited to a single post-MR assessment. - Indications for, and results of, MRI studies for the participants were not described in study. Also, the contribution if any of MRI to patients' outcomes would be difficult to establish absent a control group.

Publication	Design and Population	Intervention	Result and Conclusions:	Limitations
	Intervention: Outcome(s): - Pre- to post-MR scan changes in electrical characteristics of PM. - Occurrence of any adverse events during or after MRI in patients with PM.			

Evidence Table: (2 /16): Gimbel 1996

Publication	Design and Population	Interventions	Results and Conclusions:	Conclusion/Limitations
Authors: Gimbel JR, Johnson D, Levine PA, Wilkoff BL	Study Design: Prospective case series.	- MR scan;	Results:	Limitations noted by CMS:

Publication	Design and Population	Interventions	Results and Conclusions:	Conclusion/Limitations
Objective: To evaluate a strategy to allow a safe MR scan in PM patients. Title: "Safe performance of MRI on five patients with permanent cardiac PMs." Citation: Pacing Clin Electrophysiol 1996; 19(6): 913-9.	Participants: 5 participants underwent 5 MR scans. Age and gender information: not provided. Duration of study – Mar 1983 – June1993. Type(s) of implanted devices: All PMs were different models from the same manufacturer (Pacesetter, Sylmar, CA). Inclusion/Exclusion Criteria: Inclusion: Patients whose physician had ordered an MR scan. Outcome(s):	- Monitoring during scan for symptoms included ECG (3/5) and oximetry (1/5). A 'heavy dressing' was applied over the PM implant pocket at the discretion of the attending physician, in order to minimize the torque effect for patient comfort. - Pre- and post-scan interrogation of PM, with post-MR device reprogramming at discretion of attending physician; - Followup at 3 months post-MR included re-assessment of capture and sensing thresholds.	- No twisting or heating sensations or any other unusual symptoms were reported during or immediately after MR scans. - One individual felt their heart had stopped near the end of the MR scan. - No changes occurred to the programmed or measured parameters of the devices tested.	- Very small study (N=5) given the apparent study duration of 10 years. - Probable lack of generalizability to PMs from other manufacturers - Inconsistent application of 'strategies' to reduce risk suggests that some of the patients studied were collected retrospectively. - Absence of a 'control' group to assess effect of strategies.

Publication	Design and Population	Interventions	Results and Conclusions:	Conclusion/Limitations
	- Report of specific symptoms (including motion (torque) and warmth about the PM pocket) during and immediately after MR scan; - PM artifacts on MR image impairing interpretation of findings. - Changes in PM function after MR scan.	Indications for intervention: clinical need for MR scans for: brain or pituitary tumor (2/5); cervical disk (1/5); heart valve (1/5); CIA (1/5). Other baseline factors: - MR scans were conducted at between 0.35 – 1.5 T. - 1/5 participants was PM dependent, defined as having an escape rhythm that was hemodynamically unstable. -Indications for MR scans included: intracranial tumors (2/5); cervical disk (1/5); heart valve (1/5); and "CIA" (1/5)	- Pacing and sensing thresholds remained the same as those recorded before the MR scan. In one individual, review of the PM's event recorder showed normal pacemaker function during and scan. - MR image results from 4/5 patients were described as 'excellent'. However, in one case, artifact from the PM 'compromised' the MRI image for evaluating the patient's cardiac valve. Authors' Conclusion:	

Publication	Design and Population	Interventions	Results and Conclusions:	Conclusion/Limitations
			"When appropriate strategies are used our experience suggests that MRI may be performed, when necessary, with an acceptable risk / benefit ratio to the patient."	

Evidence Table: (3 /16): Gimbel 2005

Publication	Design and Population:	Interventions:	Results and Conclusions:	Limitations
Authors. Gimbel JR, Bailey SM, Tchou PJ, Ruggieri PM, Wilkoff BL.	Study Design: case series Population Studied: Ten PM-dependent patients underwent eleven MR scans. Age and gender information not provided. Duration of study – 1994 through 2004.	Intervention(s): -MR scan Protocol for 'safe' MRI included:	Results: - All MR scans proceeded uneventfully. No difficulties in post-MRI telemetry or interrogation were seen and no post-MRI programming changes were noted. - No patient experienced arrhythmia or symptoms during or immediately after MRI.	Limitations noted by CMS: - Generalizability to the Medicare beneficiary population is questionable due to: - Absence of age and gender information about study participants;

Publication	Design and Population:	Interventions:	Results and Conclusions:	Limitations
Objective: To determine if strategies used to safely scan non-PM-dependent patients could be applied to facilitate safe MRI of PM-dependent patients. Title. "Strategies for the Safe MRI of PM-Dependent Patients: Citation: Pacing Clin Electrophysiol. 2005; 28:1041–6.	Inclusion/Exclusion Criteria: - Inclusion: PM-dependence was defined as absence of an underlying escape rate below the lowest programmed rate of the device. - Exclusion: The protocol stipulated that patients could not undergo MRI until six weeks after PM implantation. Type(s) of implanted PMs: < Pacesetter (6); Medtronic (5). Leads were from various manufacturers.< Outcome(s): Patient signs and symptoms during MRI; electrical characteristics of MRI; MRI value for clinical question.	- Screening, reprogramming and monitoring strategies were used to facilitate MRI. – Continuous pulse oximetry as well as EKG monitoring was used to monitor the patients during the MR scans. - An electro-physiologist was present throughout each study. - The electro-physiologist and the MR technologist remained in voice contact with the patient during each procedure. - Immediate and 3-month followup.<	- Battery status remained unchanged. - No patient experienced post-MRI change in sensing thresholds. - Three/ten patients showed no change in the atrial or ventricular pacing thresholds when the pre-MRI values were compared to the immediate post-MRI values and the 3-month follow-up values. The other seven/ten patients showed a rise or fall of 0.5 V in their chamber pacing threshold values when the pre-MRI, post-MRI, and 3-month follow-up values were compared.< More patients showed a fall in their pacing thresholds than a rise post-MRI. - All MR imaging studies produced diagnostic studies for the clinical question presented by the referring physicians. No clinically significant artifacts attributable to the pacemaker were identified within the field-of-view of the MR study.	- Small sample size. Generalizability was further limited by restricting participants to those with non-thoracic MR fields: "All patients in this study had MRI exams … limited to the head and neck using a transmit receive head coil on a Siemens 1.5 Tesla Vision whole-body MR machine. This head coil limits … direct RF exposure to the IPG and its leads in the chest." Other limitations:

Publication	Design and Population:	Interventions:	Results and Conclusions:	Limitations
			Authors' conclusions: … (L)ike non-PM-dependent patients, MRI might be performed in PM -dependent patients if appropriate PM reprogramming, patient monitoring, and MR scanning techniques are implemented.	- Absence of control groups (e.g., non-PM dependent patients; matched control patients with implanted PMs not undergoing MR scans, to assess (any) changes in PM threshold values. - Absence of data on whether patient outcomes were influenced by MRI findings.

Evidence Table: (4 /16): Gimbel et al., 2005B

Publication	Design and Population	Intervention	Results and Conclusions	Limitations
Authors: Gimbel JR, Kanal E, Schwartz KM, Wilkoff BL Objective: To determine if simple strategies used to safely scan PM patients could also be applied to ICD patients.	Study Design: Case series Population Studied:	- MR scans at 1.5 Tesla. - Repro-gramming and monitoring strategies were used to facilitate MRI.	Results: - During MRI, no patient was observed while under continuous monitoring to have an arrhythmia. During MRI, six of seven patients undergoing cranial scanning reported no symptoms such as palpitations, tugging, or warmth during the scan itself.*	Noted by CMS: Generalizability of results may be compromised by - small study size

Publication	Design and Population	Intervention	Results and Conclusions	Limitations
Title: "Outcome of MRI in Selected Patients with Implantable Cardioverter Defibrillators (ICDs)" Citation: Pacing Clin Electrophysiol. 2005; 28:270–273.	Seven patients with ICDs and medical reason for MR scan. Gender and age information about participants - not provided. Duration of study –not provided Inclusion/Exclusion Criteria: - Inclusion: Patients with an ICD and a medical reason for MR scan. Indications for MR Scans: suspected posterior fossa or pituitary tumor (2/7); suspected brain metastases (2/7); or other brain lesion or symptom (3/7) Outcomes: - Adverse events during MRI	Other baseline factors: Manufacturers of ICDs were: Medtronic (6/7) and Cardiac PaceMakers, Inc. (1/7)	- Immediately after MRI, the patient's device was interrogated and no alterations of pacing, sensing, impedances, battery voltage, or charge times were noted. And with the exception of the patient undergoing the lumbar spine scan, neither was there a change in programmed parameters of the ICD post-MRI. - Follow-up interrogation data at one month post MR scan was available on six of seven patient. [One patient expired ten days post-MR scanning from complications of metastatic lung cancer—metastatic brain lesions were seen only on MRI. No ICD dysfunction was noted prior to the patient's demise.] - At one month follow-up, the six ICDs available for analysis showed no change in pacing, sensing, impedance, battery voltage, or charge time parameters.	- no demographic information, - limited long-term followup, and - absence of a control group. CMS Comment: The possible relation between an unexpected ICD reset and 'twitching' sensations in one patient, and the lumbar spine MR scan he was undergoing at the time, was not clarified.

Publication	Design and Population	Intervention	Results and Conclusions	Limitations
	- Changes in ICD parameters		* NOTE: One potentially serious adverse event occurred during a lumbar spine MR scan. One patient experienced an electrical reset or "Power On Reset" (POR) of his device. Post-MRI communication with the device was unimpaired and all pacing, sensing, impedances, battery voltages, electrograms, and charge times remained identical to the values obtained pre-MRI. The manufacturer concluded that "the cause of the POR was due to a microprocessor instruction error and/or memory error, based on a personal communication with a reliability engineer employed by the manufacturer. The authors also noted that this patient, with no other neurologic findings prior to the MR scan other than lower extremity numbness, reported "painless involuntary muscle reaction like twitching several times" of his left upper pectoral region and upper extremity during the MRI. This sensation stopped as the MR scan ended, and did not recur. Conclusions:< The authors concluded that: "Scanning of ICD patients might be performed if appropriate re-programming and monitoring is implemented."	

Evidence Table: (5 /16): Martin et al., 2004

Publication	Design and Population	Intervention	Results and Conclusions	Limitations
Authors. Martin ET, Coman JA, Shellock FG, Pulling CC, Fair R, Jenkins K Objective… To determine if patients with PMs could safely undergo MRI at 1.5-Tesla. Title. "MRI and Cardiac PM Safety at 1.5-Tesla" Citation: J Am Coll Cardiol 2004; 43: 1315–24.	Study Design: Consecutive case series (mostly prospective). Population Studied: 54 patients, with previously implanted PMs and any clinical indication for MR scan, underwent 62 MR scans (for one of which PM was 'at end-of-life'). PM performance in 61 remaining scans evaluated. Gender and age information of participants was not provided. Duration of study – December 22, 1999, through December 12, 2002 (47/54 patients); 7/54 patients included in study based on prior MR scans. Inclusion/Exclusion Criteria: Exclusions: PM-dependent patients were excluded.	- MR scans (including MR angiography (MRA)) at 1.5 Tesla. The types of MR scans included cardiac, vascular, and general MRI. No limitations were placed on the type or duration of the MRI procedure, PM, or lead models, nor proximity of the imaged anatomy relative to the PM. - All PMs were interrogated immediately before and after MR scanning, and patients were continuously monitored. Indication for MR scans: Any clinical indications for MRI (37/62), MRA (28/62) (or for both (3/62). (Note: results of MR scans, or their effects on patient management, were not indicated.) Type(s) of implanted devices: PMs from 4 manufacturers were implanted in study participants.	Results: - No episodes of loss of capture or changes in lead impedances or battery voltages were noted after MR scans. In addition, no damage to pacemaker circuits or movement of the pulse generator was observed.- - No adverse events occurred. (Two patients reported symptoms; vibration (1/54) and palpitations (1/54) coinciding "with inhibition of the pacing lead". However, termination of MR procedure was not required in either case.) - Electrocardiographic changes and patient symptoms were 'minor' and did not require cessation of MRI. - 40 (37%) of 107 (48 atrial and 59 ventricular) leads underwent changes, whereas 10 (9.4%) leads underwent a significant change. - Two of 107 (1.9%) leads required a change in programmed output.	Noted by the authors: Electro-magnetically induced noise was noted on telemetry, and it resembled serious cardiac arrhythmias. Direct effects of MRI heating were not measured; and cautioned against generalizing these findings to PM-dependent patients. Noted by CMS: - Absence of gender and age information limits generalizability to Medicare senior beneficiary population.

Publication	Design and Population	Intervention	Results and Conclusions	Limitations
	Comparison: Immediate pre- and post- MR examination of electrical characteristics of PMs, including initial programming, capture and sensing thresholds, and lead impedances. Artifacts on MR images were noted.< Outcome(s): - 'Any change' and 'any significant change' in pacing thresholds after MR, each assessed as 'yes/no'. [Any change was determined in patients with any measurable difference in either an atrial or ventricular lead; any significant change was determined with measurable differences exceeding 1 voltage or pulse width increment or decrement.		- Threshold changes were unrelated to cardiac chamber, anatomical location, peak SAR, and time from lead implant to the MRI examination. < Conclusion: The authors concluded that safety was demonstrated in this series of patients with pacemakers at 1.5-T. They also discussed the clinical significance of the PM threshold changes observed. Significant changes were infrequent … The energy increases that were needed to accommodate the rise in thresholds were minor and did not impair the safe performance of the pulse generators. Despite the labeling of these changes as significant, they were of no clinical consequence.	- Data from seven participants were retrospectively collected. - Lack of information on results of MR scans or of their impact of patient outcomes prevents any conclusions of MRI in patients' overall care.

Evidence Table: (6 /16): Naehle 2006

Publication	Design and Population	Intervention	Results and Conclusions	Limitations
Authors: Naehle CP, Sommer T, Meyer C, Strach K, Kreuz J, Litt H, Lewalter T, Schild H, and Schwab OJ. Objective: "To report on an MRI performed on a patient with an ICD, in which full function of the ICD system was verified after imaging". Title. "Strategy for Safe Performance of Magnetic Resonance Imaging on a Patient with ICD". Pacing Clin Electrophysiol 2006; 29: 113–116.	Study Design: Case report. Participants: 1, a 33 y.o. male with past history of astrocytoma and suspected recurrence, for whom imaging could not be done with alternative radiologic methods.	Intervention: - Clinical need: evaluate for suspected astrocytoma recurrence. - MR scan at 1.5 T. - Imaging hardware and protocols were modified to minimize radiofrequency power deposition to the ICD system. Primary reason for intervention: Assess possible recurrent astrocytoma.	Results: - "The patient underwent the MRI safely and without any discomfort, such as heating sensation or movement of the device. No cardiac arrhythmia was observed during the exam. - "ICD interrogation immediately after MRI showed that no ventricular arrhythmia detection occurred, and that the ability to interrogate, program, or use telemetry was unaffected. The ICD did not undergo an electrical reset. Complete ICD evaluation was performed immediately before and after, 3 days after, and 6 weeks after the MRI including measurement of sensing, PCT, lead impedance, and battery voltage. PCTs remained stable, and other parameters showed only mild alterations, all within the margin of error of the measurements. … A test of ICD integrity was performed 3 days after MR scan. VF was induced, and the ICD sensed the VF properly and terminated the arrhythmia with a 20-J shock, unchanged from the implantation procedure in 2004.	Limitations noted by CMS: - Single case report.

Publication	Design and Population	Intervention	Results and Conclusions	Limitations
		Type(s) of implanted devices: Biotronik Lexos VR ICD	- "Serum troponin was 0.02 ng/mL before and 0.00 ng/mL after the procedure, without any evidence of MRI-related myocardial damage."	
		Outcomes:	Conclusions:	
		Patient-reported sensations or symptoms; electrical characteristics of ICD before MRI, and immediately and 6 weeks after MRI; before and after MR scan serum troponin levels; impact of MR results on patient's therapy.	- No evidence of adverse effects to the patients was noted during or after MRI. Patient was referred for chemotherapy for recurrent astrocytoma.	
			- "A complete ICD check is required before and immediately after MRI. Moreover, we strongly recommend performing an ICD device test, including induction of VF after the MRI to ensure a fully competent ICD system. Additional testing, that is, an ICD follow-up 6 weeks after MRI, should be performed to assess potential late effects."	

Publication	Design and Population	Intervention	Results and Conclusions	Limitations
Authors. Naehle CP, Strach K, Thomas D, Meyer C, Linhart M, Bitaraf S, Litt H, Schwab JO, Schild H, and Sommer T. Objective: To establish and evaluate a strategy for safe performance of magnetic resonance imaging (MRI) at 1.5-T in patients with implantable cardioverter-defibrillators (ICDs) Title. "Magnetic Resonance Imaging at 1.5 -T in Patients With Implantable Cardioverter-Defibrillators" Citation:	Study Design: Prospective case series Population Studied: Eighteen patients implanted for at least 3 months undergoing MR scans at 1.5 T. Their mean age was 61.8 yr. (range: 35-84 yr.) Gender information: not provided. Inclusion/Exclusion Criteria: Inclusion: - Urgent need for an MRI examination;	Intervention(s): - reprogramming of ICD pre-MR scan, as per protocol; - 1.5 Tesla (T) MR scan; - < patient symptom report during MR scan; - pre- and post-scan sampling of patient troponin level; - pre- and post-scan ICD interrogation;	Results: None of the following were observed: - MR scan termination; - patient-reported sensations; - heart rate or rhythm variations or arrhythmias; - electrical reset of ICDs; - for troponin levels, significant change or elevation above the upper limit of the reference interval (0.1 ng/mL).	Limitations noted by CMS: - This small study does not comment on the quality of MR images or their impact on the patient's care or outcome.

Publication	Design and Population	Intervention	Results and Conclusions	Limitations
J Am Coll Cardiol 2009; 54: 549–55.	- Presence of an ICD system; at least six months' estimated battery life; - Pacing lead impedances 200 to 2,000 ohms; shock lead impedance 10 to 80 ohms; - Stable pacing parameters: pacing capture threshold < 2.5 V at a pulse duration of 0.4 ms; Sensing > 5 mV; min. three mo. since ICD and lead implantation Exclusion: unstable angina; myocardial infarction within the previous 3 months; cardiothoracic surgery within the previous 3 months; pacemaker dependency (defined as an intrinsic heart rate _50 beats/min); presence of MRI incompatible bioimplants or other MRI incompatible materials; presence of abandoned leads	- ICD reprogramming post-MR to baseline; - 3 month followup.	Two parameters were reported to change significantly in the pre-MR to post-MR comparisons: - Battery voltage changed slightly (3.86 +/- 1.48 pre-MR to 3.83 +/- 1.51 post-MR) but was reported to be statistically significant. - Capacitor charging time decreased (from 11.2 +/- 4.9 s pre-MR to 9.5 +/- 4.28 post-MR). Author's Conclusion: "MRI of non–pacemaker-dependent ICD patients can be performed with an acceptable risk/benefit ratio under controlled conditions by taking both MRI- and pacemaker-related precautions."	

Publication	Design and Population	Intervention	Results and Conclusions	Limitations
	Other baseline factors: - Manufacturers (number) of implanted devices: Medtronic (8); Guidant (4), Biotronik (3); other (3). Outcome(s) assessed: - Changes in ICD parameters - Patient symptoms during MR related to movement or heat or any other sensation. - Pre- and post-MR troponin levels.			

Publication	Design and Population	Intervention	Results and Conclusions	Limitations

Evidence Table (8 / 16): Naehle et al., 2009

Publication	Design and Population	Intervention	Results and Conclusions	Limitations
Authors. Naehle CP, Zeijlemaker V, Thomas D, Meyer C, Strach K, Fimmers R, Schild H, and Sommer T. Objective: To evaluate possible cumulative effects of repeated MRI examinations on pacemaker systems in patients with cardiac pacemakers.	Study Design: Retrospective case series Population Studied: 47 patients with PMs who underwent 2 or more MRI examinations at 1.5 T in any anatomical region. These 47 patients underwent a total of 171 MR scans, with median of 2 MR scans per patient was 2; however, three patients underwent 12, 13, and 18 MR scans. Patients' age and gender information was not provided. Period of study eligibility– October 2000 - February 2008	- Patients underwent different types of MR scans, including brain (107/171); lumbar spine (27/171); and other anatomical regions (38/171) - Pacemakers were interrogated before and after MR imaging, and after 3 months; pacing capture threshold, lead impedance, and battery voltage were measured.	Results: - Atrial pacing capture thresholds (PCT), both pre- and post-MR PCTs and PCT on 3-month followup decreased by less than .01 volt (V) (C.I. -0.0193 - -.0001) with increasing number of MR scans. None of the 37 patients with an atrial pacing lead had a change in PCT of 1.0 V or more. - Based on data from 43 patients with ventricular pacing leads, both pre- and post-MRI and 3-month followup, there was a small (-0.01- -0.02 V) decrease in ventricular PCT with increasing MR scans. None of these 43 patients had a change in ventricular PCT of 1.0 V or more.	Limitations noted by CMS: There is potential for selection bias in a retrospective case series. Limitations noted by authors:

Publication	Design and Population	Intervention	Results and Conclusions	Limitations
Title. "Evaluation of Cumulative Effects of MR Imaging on Pacemaker Systems at 1.5 Tesla" Citation: Pacing Clin Electro-physiol. 2009; 32:1526–1535.	Inclusion/Exclusion Criteria: - Inclusion:< an urgent need for an MRI examination, stable physical PM parameters (estimated remaining battery lifetime >6 months, LIs 200 to 2,000 ohms), stable pacing parameters (PCT <2.5 V at a pulse duration of 0.4 ms, sensing >5 mV), and 3 or more months since PM and lead implantation.< - Exclusion criteria were absolute PM dependence, presence of MRI-incompatible bioimplants or other MRI incompatible materials, and history of ventricular tachycardia or fibrillation. Implanted devices: PMs from eight manufacturers were implanted in the 47 study participants. Outcome(s):	To minimize the risk for RF related heating, the specific absorption rate was limited to 1.5 W/kg, and the scanning sequences were modified (as) necessary.	- Lead impedance (LI) was not changed significantly based on number of MR scans. None of the patients' atrial or ventricular LI exceeded expected limits (200 – 2000 ohms). - Battery voltages (BV) showed a small but significant decrease as a function of number of MR scans received. The absolute changes in pre-MR, post-MR and followup BV was about 0.001 V/MR scan. However, these changes were less than the accuracy of the measurement. Also, mean BV decreased by 0.01V/yr. Conclusion: No clinically relevant, cumulative changes in PCT, LI, or BV could be detected in PM patients who underwent two or more MRI examinations.	The authors commented that, in the PMs studied, the programming of PCT is limited by pre-set voltage steps, e.g., 0.1V. Also, the method and precision of voltage measurements in these devices was not clarified. At one point authors mentioned 30% margin of error. Finally, in the few patients who underwent a dozen or more MR scans, the validity of using linear regression models of PM parameter behavior was questioned. However, the authors did suggest that further clinical studies of cumulative effects would be valuable.

Publication	Design and Population	Intervention	Results and Conclusions	Limitations
	- PM electrical characteristics were compared by regression analysis for changes with # of MR scans, and with time.			

Evidence Table; (9 / 16): Nazarian et al., 2006

Publication	Design and Population	Intervention	Results and Conclusions	Limitations
Authors. Nazarian S, Roguin A, Zviman MM, Lardo AC, Dickfeld TL, Calkins H, Weiss RG, Berger RD, Bluemke DA, and Halperin HR. Objective: Assess - the immediate & long-term safety of MRI protocol for patients with permanent PM or ICD and - the diagnostic yield of MRI in this setting.	Study Design: Prospective case series (uncontrolled). Population Studied: N=55. 31/55 had an implanted PM, with 12/31 PM-dependent; 24/55 had an implanted ICD. Duration of study – February 2003 to September 2005. Age and gender information about participants was not provided. Inclusion/Exclusion Criteria:	Interventions - MR scans with safety protocol and concurrent monitoring. - Pre- and post -scan interrogations of implanted devices; long-term followup; review of images from MR scans.	- No symptoms consistent with device movement, torque, or heating were reported during MRI examinations. - No inappropriate inhibition of pacing was observed during MRI. In (10) permanent PM without magnet-mode programming capability, reed switch activation by the static magnetic field of MRI led to transient asynchronous pacing at the device-specific magnet rate (85 pulses/minute), which ceased on patient positioning in the magnet bore. -No unexpected or rapid activation of pacing was observed during MRI. All devices were functioning appropriately after MRI, and no changes in device programming were observed.	Noted by authors: transient reed switch activation, a part of normal device function, has minimal to no clinical consequences. Also, the authors cautioned that no cardiac devices had (as of 2006) achieved industry or Food and Drug Administration clearance for MRI compatibility, and catastrophic complications have been reported.

Publication	Design and Population	Intervention	Results and Conclusions	Limitations
Title. "Clinical Utility and Safety of a Protocol for Noncardiac and Cardiac MRI of Patients With PMs and ICDs at 1.5 Tesla" *Circulation*. 2006; 114: 1277 -1284.	Inclusion: clinical indication for MRI, no acceptable imaging alternative, with an implantable cardiac device. Patients were enrolled in the study if the permanent PM or ICD was found to be safe by previous in vitro phantom and in vivo animal testing. Exclusion: Patients with device implantation less than 6 weeks before MRI and those with nontransvenous epicardial leads, no fixation (such as superior vena cava coil), or abandoned leads were excluded. Outcome(s): - Primary: Changes in electrical characteristics of PMs, ICDs - Secondary: Ability of MR scan images to answer clinical questions.	55 patients underwent 68 MR scans. More frequent indications included: vascular malformation or disease (23/55); staging of malignancy (9/55).	- 4 patients died before discharge from the index admission; 2 others had device upgrades implanted, 2 others had devices explanted after MRI. 29 of 47 remaining patients had chronic device interrogation with median followup time of 99 days. No significant differences in device parameters were found at followup in these 29/47 patients. - Answers to clinical questions were successfully determined in 27 of 29 (93%) thoracic MR scans, and in all 39 (100%) non-thoracic MR scans. Conclusion: "… MRI can be performed safely in patients with certain permanent pacemaker or ICD systems. When proper precautions are taken, MRI of the region that contains the device is not associated with increased risk. This ability may significantly impact clinical decision making in appropriate patients… "	Noted by CMS: These results may be difficult to generalize to either implantable devices not tested for susceptibility to EM effects or to MR scanners, other than those devices or scanners used in the present study. Also, absence of age information on subjects makes generalizability to Medicare senior population more difficult to assess. Finally, the study did not include information about patient outcomes due to MRI information in clinical management; and there was no control group to indicate the contribution of MRI in patient outcomes.

Publication	Design and Population	Intervention	Results and Conclusions	Limitations

Evidence Table: (10 / 16): Sommer et al., 2006

Publication	Design and Population	Intervention	Results and Conclusions	Limitations
Authors: Sommer T, Naehle CP, Yang A, MD; Zeijlemaker V, Hackenbroch M, Schmiedel A, Meyer C, Strach K, Skowasch D, Vahlhaus C, Litt H, and Schild H Objective: Evaluate strategy for safe performance of extra-thoracic MRI in non-PM-dependent patients with cardiac PMs. Title. "Strategy for Safe Performance of Extrathoracic MRI at 1.5 Tesla in the Presence of Cardiac PMs in Non–PM-Dependent Patients: A Prospective Study With 115 Examinations".	Study Design: Prospective consecutive case series Participants: 82 PM patients were studied (of 103 patients originally recruited); these 82 patients underwent 115 MRI examinations at 1.5T. Age and Gender: Mean age was 66.9 yr old (range 4 – 89 yr.); 53 males, 29 females participated. Inclusion/Exclusion Criteria:	Intervention(s): - To minimize radiofrequency-related lead heating, the specific absorption rate was limited to 1.5 W/kg. - All PMs were reprogrammed before MRI based on pre-scan pulse: If heart rate was < 60 bpm, the asynchronous mode was programmed to avoid magnetic resonance (MR)–induced inhibition; if heart rate was > 60 bpm, sense-only mode was used to avoid MR-induced competitive pacing and potential proarrhythmia.	- All MR examinations were completed safely. - Inhibition of pacemaker output or induction of arrhythmias was not observed. - PCT increased significantly from pre- to post-MRI (P = =0.017). In two of 195 leads, an increase in PCT was only detected at follow-up.	Noted by CMS: - All devices investigated were from a particular manufacturer. This might limit the results and conclusions of the study as being valid only for that manufacturer's pacemakers. - Generalization of this data, on safety of extra-thoracic MRI, may not easily be generalized to MR examinations of the thorax, or to MR scans of PM-dependent patients.

Publication	Design and Population	Intervention	Results and Conclusions	Limitations
Circulation. 2006 Sep 19; 114: 1285 - 1292.	Inclusion: Presence of a cardiac PM and urgent clinical need for an MRI examination. Exclusion: PM-dependent patients (9/103) and those requiring examinations of the thoracic region (12/103) were excluded. Also, presence of MRI-incompatible bioimplants, or presence of other MRI-incompatible materials were exclusion criteria. Type(s) of implanted devices: Various models of Medtronic PMs, and various models of atrial and ventricular leads from a variety of manufacturers (Medtronic, Guidant, Biotronik, St. Jude Medical, etc.) were implanted in participants. Outcome(s): Safe completion of MR scan; report of symptoms during or after MRI; changes in electrical characteristics of PMs.	- During the MR scan, audio contact was established via an intercom system, and patients were asked to inform the investigator immediately of any torque or heating sensation, palpitations, dizziness, pain, or other unusual symptoms during imaging. - An electrophysiologist and full resuscitation equipment were present during all examinations.< Patients were monitored with ECG and pulse oximetry. - All PMs were interrogated immediately before and after the MRI examination and after 3 months, including measurement of pacing capture threshold (PCT) and serum troponin I levels.	- In four of 114 examinations, troponin increased from a normal baseline value to above normal after MRI. In one case (troponin pre-MRI 0.02 ng/mL, post-MRI 0.16 ng/mL), this increase was associated with a significant increase in PCT. - After MR scan, six patients died at a mean interval of 58 days (range 42 to 81 days) after MRI. All deaths were related to the underlying disease (melanoma with cerebral metastases, pancreatic carcinoma, and brain tumors (4)). None of the six deaths was classified as pacemaker or MRI related. Conclusion: Extrathoracic MRI of non–PM-dependent patients can be performed with an acceptable risk-benefit ratio under controlled conditions and by taking both MR- and PM-related precautions.	- The contribution, if any, of MRI in improving patient outcomes is difficult to establish in the absence of a control group. - Interpretation of the change in troponin levels is difficult without a control group.

Publication	Design and Population	Intervention	Results and Conclusions	Limitations

Evidence Table, CMS Internal Literature Review: (11 / 16): Al-Sabagh et al., 2010

Publication	Design and Population	Interventions	Results and Conclusions	Limitations
Authors: Al-Sabagh KH, Christensen BE, Thorgersen AM, Petersen HH, Videbaek R, Pehrson S, Chen X, Thomsen C, and Svendsen JH. Objective: Investigate safety and effects of MR scanning in patients with PM and ICD with indications for MRI. Title. "Safety of MR scanning of patients with PMs and implantable defibrillators."	Study Design: case series. Participants: 65 patients. Age and Gender: Age information not provided. Participants included 46 men and 19 women. Inclusion Criteria: Patients with implanted PM or ICD and a clinical indication for MRI.	65 patients underwent 73 MR scans at 1.5 T. There were no limitations on scan area; Peak specific energy absorption rate was limited to 1.5 Watts/kg. During scans, patients were monitored by telemetry, oximetry, and plethysmography; occurrence of ectopic beats was monitored by an electrophysiologist. Patients were encouraged to mention any symptoms or unusual sensations during MR scanning.	- Indications for MR scanning were mostly for brain or spinal cord injury. - Two MR examinations were interrupted due to serious clinical events: (1) bradycardia due to low battery voltage, and (2) ICD reset during MR scan with subsequent atrial fibrillation and cardiac arrest in another patient with ICD. No other patients had an adverse clinical event related to the scan. - One artifact related to an implanted PM was noted during a thoracic spine MR scan.	The authors noted that only two manufacturers were the predominant sources of implanted units in their patients, raising a question about generalizability of their findings to other sources. Also, the authors noted the absence of information on long-term effects of MR scans on patients.

Publication	Design and Population	Interventions	Results and Conclusions	Limitations
Citation: Ugeskrift for laeger 2010 Jun 7; 172(23): 1740-4	Exclusion Criteria: None indicated. Types of Implanted Devices: 60 of 65 patients had implanted PMs; 5 had implanted ICDs. Devices from four manufacturers were implanted in study participants. Total number of leads was 101. Outcome(s): - Changes in pacing thresholds, electrode impedance before and after MR scanning. - A clinically significant change of the pacing threshold was defined as $\geq$ 1 Volt of threshold elevation.		- A clinically significant elevation of a pacing capture threshold was noted to affect one atrial lead in one patient. - A significant drop was noted in atrial lead impedance (from 556 +/- 220 ohms to 542 +/- 223 ohms).	Finally, the authors recognized that the number of ICD patients (n=5) was small and might have little evidentiary weight relative to MR scanning safety.

Publication	Design and Population	Interventions	Results and Conclusions	Limitations

Evidence Table, CMS Internal Literature Review: (12 / 16): Burke et al., 2010

Publication	Design and Population	Interventions	Results and Conclusions	Limitations
Authors: Burke PT, Ghanbari H, Alexander DB, et al. Objective: Assess use of a safety protocol for MR scanning of implanted cardiac devices	Study Design: prospective case series. Participants: 38 patients with an indication for MRI. Age and Gender: Not available. Inclusion/Exclusion Criteria:	- Participants underwent a total of 92 MR scans performed at 1.5 T, using an institutionally-developed safety protocol: - an electrophysiologist was immediately available during each MR scan; - except for PMD patients, each implantable device was switched before the scan to non-tracking, non-pacing mode; - all ICD therapies were turned off; external PM, defibrillator, and resuscitation equipment were available on site;	- Of the 92 scans performed, spine (any area) (n-44), brain (n=37), and lower extremities and pelvis (n=11) were imaged. - Mean scan duration was 26 minutes - No patient experienced any unusual or noxious symptoms during the scan.	Noted by authors:

Publication	Design and Population	Interventions	Results and Conclusions	Limitations
Title. "A protocol for patients with cardiovascular implantable devices undergoing magnetic resonance imaging (MRI): should defibrillation threshold testing be performed post-(MRI)". J Interv Card Electrophysiol. 2010 Jun; 28(1): 59-66.	Types of Implanted Devices: 24 patients had PMs; 10 had ICDs; 4 had cardiac resynchronization therapy with defibrillation (CRT-D). Outcome(s): Completion of MR scan; presence of image quality limiting artifacts attributed to implanted device; patient symptoms or electrophysiological abnormalities; changes in electrical parameters of devices immediately after MR scan and at three month followup.	- blood pressure and oximetry results were monitored closely during the MR scans; - MR staff were in verbal communication with the patients at all times during the MR scans; - and post-MR scan interrogation and re-programming of CIEDs to pre-scan parameters. -	- No electrophysiological abnormalities such as arrhythmias were noted. - All scans were successfully completed and free of image quality limiting artifact attributed to the implanted device. - Pacing thresholds and rate settings after MR scans were unchanged from pre-MR values. No post-MR changes in device electrical characteristics were observed. The authors concluded that MR scanning of patients with implanted devices was safe and effective. They also concluded that there was no need for device reprogramming after MRI.	

Publication	Design and Population	Intervention	Results and Conclusions	Limitations
Authors: Mollerus M, Albin G, Lipinski M, et al. Objective: Detect changes in cardiac biomarkers in patients with implanted PMs or ICDs during MR scan . Title. "Cardiac biomarkers in patients with permanent pacemakers and implantable cardioverter-defibrillators undergoing an MR scan." Citation: Pacing Clin Electrophysiol. 2008 Oct; 31(10): 1241-5.	Study Design: prospective case series. Participants: 37 patients. Age and Gender: Not provided. Inclusion Criteria: Patient's baseline cardiac rhythm was sinus rhythm; the magnet mode on the implanted device could be disabled.	37 patients underwent 40 MR scans at 1.5 T. There were no limitations on scan area or on peak specific absorption rate. During scans, patients were monitored by telemetry, oximetry, and plethysmography; occurrence of ectopic beats was monitored by an electrophysiologist.	- No significant pre- to –post-MR scan changes in either troponin-I or myoglobin. - Pacing capture thresholds also remained unchanged. - No patient had an adverse clinical event related to the scan. The authors concluded that no observable indications of myocardial necrosis occurred during the MR scans.	

Publication	Design and Population	Intervention	Results and Conclusions	Limitations
	Exclusion Criteria: Patient's device was implanted less than six weeks before MRI; patient's native ventricular rate was less than 40 bpm; an epicardial lead was present; or having an implanted device with known increased risk from MR scan exposure. Types of Implanted Devices: Outcome(s): - Occurrence of ectopic beats during MR scanning; - changes in cardiac troponin-I and myoglobin immediately after scan and after 6-12 hours;			

Publication	Design and Population	Intervention	Results and Conclusions	Limitations
	- changes in devices electrical characteristics post-MR scan.			

Evidence Table, CMS Internal Literature Review: (14 / 16): Mollerus et al., 2009

Publication	Design and Population	Intervention	Results and Conclusions	Limitations
Authors: Mollerus M, Albin G, Lipinski M, et al. Objective: Detect ectopic cardiac beats during MR scans of patients with implanted PMs or ICDs. Title. "Ectopy in patients with permanent pacemakers and implantable cardioverter-defibrillators undergoing an MR scan."	Study Design: prospective case series. Participants: 52 patients with implanted PMs or ICDs. Age and Gender: Information not provided.	52 patients with 119 leads underwent 59 MR scans. Anatomic areas scanned included: - 33 were of the head;	- Onset of atrial fibrillation during the scan was noted in one patient.	

Publication	Design and Population	Intervention	Results and Conclusions	Limitations
Citation: Pacing Clin Electro-physiol. 2009 Jun; 32(6): 772-8.	Inclusion Criteria: Patient's baseline cardiac rhythm was sinus rhythm; the magnet mode on the implanted device could be disabled. Exclusion Criteria: Patient's device was implanted less than six weeks before MRI; patient's native ventricular rate was less than 40 bpm; an epicardial lead was present; or having an implanted device with known increased risk from MR scan exposure. Types of Implanted Devices: 46 devices were PMs; six devices were ICDs. Outcome(s):	- 29 were of the trunk including lumbar spine. (one scan included both areas). (The authors noted that, per protocol, 29 MR scans were excluded from analysis due to baseline ectopy, pre-existing atrial fibrillation or flutter; or inability to disable magnet mode in the implanted device.)	- Seven of 52 patients had significant ectopy observed either by telemetry or by oximetry monitoring when MR artifact interfered with telemetry interpretation. Significant ectopy was found in five head scans, and two truncal scans. In these seven patients, significant ectopy was noted during various phases of MR scanning, including: T1 spin echo, T1 turbo spin echo, T2 turbo spin echo, fluid-attenuated inversion recovery and diffusion scans. In five of seven patients with significant ectopy, the ectopic source was ventricular; in the other two, MR artifact made interpretation of the source of the ectopic beat impossible. The median peak SAR was 2.6 watts/kilogram, ranging from 1.3 to 3.2 W/kg. No significant association between peak SAR and presence of significant ectopy was noted.	

Publication	Design and Population	Intervention	Results and Conclusions	Limitations
	- Electrophysiological abnormalities or ectopy occurring during the MR scan. "Significant ectopy" was defined as 20 or more ectopic beats during the entire scan.		The authors concluded that a minority of patients with implanted pacemakers may have MRI-related ectopy. They suggested that in four of seven patients with significant ectopy during MR scans, timing of ectopic beats suggested that the pacemaker's noise-rejection behavior may result in asynchronous pacing due to excessive EM noise from the MR scanner.	

Evidence Table, CMS Internal Literature Review (15 / 16): Mollerus et al., 2010

Publication	Design and Population	Intervention	Results and Conclusions	Limitations
Authors: Mollerus M, Albin G, Lipinski M, & Lucca J.	Study Design: prospective case series. Participants: 103 patients with implanted PMs or ICDs.	103 patients with 240 total leads underwent 127 MR scans. 62 MR scans included at least one landmark in the trunk.	- For all scans, the median (25th and 75th percentiles) peak SAR was 2.5 (1.3, 3.2) W/kg whereas the median scan time was 1650 (1236, 2099) seconds.	The authors cautioned that - the study was not sufficiently powered to detect low-frequency adverse events; and that

Publication	Design and Population	Intervention	Results and Conclusions	Limitations
Objective: Investigate if medically necessary MRI scans can be performed safely on patients with implanted PMs or ICDs without limiting specific absorption rate (SAR). Title. "MRI of pacemakers and ICDs without specific absorption rate restrictions." Citation: Europace 2010 July; 12(7): 947-51.	Age and Gender: Information not provided. Inclusion Criteria: Referred by their healthcare providers for MRI scan; implanted PM or ICD in place for at least six weeks. Exclusion Criteria: Patient's device was implanted less than six weeks before MRI; patient's native ventricular rate was less than 40 beats per minute; an epicardial lead was present; a known or suspected lead fracture was present; battery status was at end of life or elective replacement indicated; or having an implanted device with known increased risk from MR scan exposure.	The authors noted that: - if possible to do so, magnet mode was disabled during the scans; and - if an ICD was present, therapy features were disabled during the scans. All scans were performed using a single model of a 1.5 T scanner from one manufacturer.	- Pre- and post-scan pacing thresholds were unchanged [0.7 (0.5, 0.8) vs. 0.6 (0.5, 0.8) Volts at 0.5 ms, P = NS], though the sensed amplitudes [6.7 (2.9, 11.5) vs. 6.1 (2.9, 11.2) millivolts, P < 0.0001] and pacing impedances [500 (440, 609) vs. 491 (437, 593) ohms, P < 0.0001] both decreased significantly. No significant changes in battery status were seen immediately following a scan. A number of adverse events were reported: - One patient experienced the onset of atrial fibrillation during a scan (This patient had been cited previously in Mollerus 2009). -One pacemaker had a 'device reset' which required reprogramming. - One ICD had its arrhythmia log erased during a scan.	- the study's results should not be extended to pacemaker-dependent patients. [Additional note: the first author subsequently clarified (Europace 2010 Dec; 12(12): 1798 (e-published August 14, 2010)) that the term 'peak' as used in this study referred to "… the maximum value for a given sequence of scans for a specific patient session. For example, if scan session values ranged from 0.8 to 2.0 W/kg, then 2.0 W/kg was reported. The recorded SAR was from the console reading of the Siemens Symphony scanner, which reports SARs differently from other manufacturers."

Publication	Design and Population	Intervention	Results and Conclusions	Limitations
	Types of Implanted Devices: 109 devices were PMs; 22 devices were ICDs. Outcome(s): - Electrophysiological abnormalities, altered electrical characteristics of battery or lead, or ectopy occurring during the MR scan.		No significant study-related events were seen at the 3-month follow-up. The authors concluded that, based on this series of patients' results, MRI scans may be performed safely in appropriately selected patients up to a peak SAR of 3.2 W/kg. Furthermore, peak SAR level poorly predicts the safety profile of pacemakers or ICDS exposed to an MRI environment.	

Evidence Table, CMS Internal Literature Review: (16 / 16): Schmiedel et al., 2005

Publication	Design and Population	Intervention	Results and Conclusions	Limitations
Authors: Schmiedel A, Hackenbroch M, Yang A, Naehle CP, Skowasch D, Meyer C, Schimpf R, Schild H, Sommer T.	Study Design: case series.	45 patients underwent 63 MR scans at 1.5 T. MR scans were limited to the brain. Peak specific energy absorption rate was limited by study design to 1.2 Watts/kg.	No patients reported any symptoms during the MR scans.	

Publication	Design and Population	Intervention	Results and Conclusions	Limitations
Objective: To investigate the MR-compatibility of PMs in a 1.5 T system in examination of brain. Title. "MRI Examinations of the Brain in Patients with Implanted PMs. Experimental and Clinical Investigations Using a 1.5 Tesla System" Citation: Fortschr Roentgenstr 2005; 177: 731-44. (CMS Note: In vitro assessments of PM response in an MR environment using patient simulating phantoms were not included in this table.)	Participants: 45 patients. Age and Gender: Not provided. Inclusion Criteria: Patients with implanted PM and a clinical indication for MRI. Exclusion Criteria: None indicated.	During scans, patients were monitored by telemetry and pulse oximetry. Patients were encouraged to mention any symptoms or unusual sensations during MR scanning.	Comparison of PM and lead characteristics pre - and post-MR scan showed no changes, and all devices were able to be re-programmed to original device settings without difficult. No arrhythmias related to PM function were observed during MR scans. The authors concluded that there was no indication of damage to PM components associated with MR scanning at 1.5 T for brain examination with suitable examination strategies and precautions.	The authors noted that the results of this study were derived from a particular 1.5 T system from one manufacturer. Therefore, generalizability of findings to other MR systems may be limited in the absence of further studies.

Publication	Design and Population	Intervention	Results and Conclusions	Limitations
	Types of Implanted Devices: All patients had implanted PMs. Devices from twelve manufacturers were implanted in study participants. Total number of leads was 106. PMs were programmed before MR scan to asynchronous mode (XOO). Outcome(s): - Changes in pacing thresholds, battery voltage, electrode impedance and programmed device settings were measured before and after MR scanning.		Also, they noted the opening of the PM's reed switch occurred in a majority of patients during the MR scan, and that this could be a danger to the patient.	

APPENDIX C

INSTRUCTIONS FOR SUBMISSION OF APPLICATIONS FOR PROTOCOLS TO ADDRESS CED AS REQURED BY AN NCD

Please complete the sections below entitled "Required Information" and "NCD/CED Coverage Requirements," and return to CMS for review (see email and mailing addresses below). Electronic submissions are preferable.

After preliminary review of the application (and any attached documentation) CMS will electronically notify the principal investigator (or the designated contact person) that we have received the application with all required information. Alternatively, we will request further information about an application with incomplete items.

The information provided in the sections on the following pages pertains to clinical research studies which intend to qualify for CED as specified in the NCD on Magnetic Resonance Imaging (CAG-00399R2) issued in final form on February 24, 2011 by CMS.

If the information provided fulfills these NCD requirements as judged by CMS, then Magnetic Resonance Imaging for patients with implanted PMs or ICDs required by the study may be reimbursable for study participants who are Medicare beneficiaries, pursuant to §1862(a)(1)(E) of the Social Security Act. If CMS approves the study, we will provide billing instructions for Medicare reimbursement of Magnetic Resonance Imaging (MRI) in patients with implanted PMs or ICDs under CED.

Within 90 days of receipt of a completed application, we will send the results of CMS' review of the application. There are three possible outcomes of the review process: accept, revise, and reject. If we request a revision, the applicant must submit the revision within 30 days of notification. CMS will review the revised application and notify the applicant of our final decision within 30 days of receipt of the revised application.

REQUIRED INFORMATION

1. **Date of submission**
2. **Descriptive title**
3. **Contact information:**
    - Name and title of principal investigator (PI)
    - Name and title of contact person if other than the PI
    - PI's (or contact person's) mailing address, telephone number, fax, and email address
    - Institutional or organizational affiliation
    - Study sponsor(s)
4. **Brief annual updates or websites that CMS may access to get the information below:**
   Please send updates electronically to leslye.fitterman3@cms.hhs.gov (or the mailing address below) that contain the following information about Medicare patients enrolled in the study:

- Number screened
- Number enrolled
- Reason for non-enrollment
- Number of dropouts
- Reason for dropout
- Number with completed data collection
- Progress of data analysis
  - Analysis file constructed (y/n)
  - Analyses to address each hypothesis completed (y/n)
- Manuscript completed (y/n)
- Manuscript sent to journal (date)

NCD/CED COVERAGE REQUIREMENTS

CMS will review and evaluate the protocol to ensure that the proposed study protocol meets the following requirements.

a. **Study population: qualifications for study**

The protocol should describe the criteria for Medicare beneficiaries to be included and excluded from the study.

b. **Evaluation of outcomes**

The protocol should define each outcome to be studied and explain method(s) and timing(s) of outcome assessment(s). The description should include expected length of follow up for participants. The study sample size and duration should allow for reliable estimate(s) of all outcome endpoints.

At minimum, the outcomes to be studied must include one of the following for the study to be eligible for coverage:

For physician decision making:

- Clinical management strategy,
- Planning of treatment interventions,
- Prevention of unneeded diagnostic studies or interventions, or preventable exposures,

Or, for patient outcomes related to:

- Survival,
- Quality of life, or
- Adverse events during and after MR scanning

c. **Standards of scientific integrity and relevance to the Medicare population**

Note: Please include a specific reference to the page or pages in your application with your response to the following.

a. The principal purpose of the research study is to test whether a particular intervention potentially improves the participants' health outcomes.

   - *Describe how you will measure the outcomes listed in the NCD.*

b. The research study is well-supported by available scientific and medical information or it is intended to clarify or establish the health outcomes of interventions already in common clinical use.

   - *Provide a brief review of pertinent published research that supports your study hypotheses and methods.*

c. The research study does not unjustifiably duplicate existing studies.

   - *Justify that your study adds to existing evidence.*

d. **The research study design is appropriate to answer the research question being asked in the study.**

The response to this Standard should contain the following:

- Introduction
- Hypotheses to be tested
- Specific aims
- Background and significance
- Trial design
- Target population and recruitment target
- Inclusion/exclusion criteria
- Power calculations
    - a. Effect size
    - b. Basis of selected effect size

The research study must meet one or more aspects of the following questions:

1. Do results of MRI in PM/ICD beneficiaries with implanted cardiac devices affect physician decision making related to:

    a. Clinical management strategy (e.g., in oncology, toward palliative or curative care)?
    b. Planning of treatment interventions? ; or
    c. Prevention of unneeded diagnostic studies or interventions, or preventable exposures?

2. Do results of MRI in PM/ICD beneficiaries with implanted cardiac devices affect patient outcomes related to:

    a. Survival?
    b. Quality of life? ; or
    c. Adverse events during and after MR scanning?

e. **The research study is sponsored by an organization or individual capable of executing the proposed study successfully.**

- *Provide CVs of investigators with a description of their contribution to the project.*
- Describe the capabilities of the study sites.

f. **The research study is in compliance with all applicable Federal regulations concerning the protection of human subjects found in the Code of Federal Regulations (CFR) at 45 CFR Part 46. If a study is regulated by the Food and Drug Administration (FDA), it also must be in compliance with 21 CFR Parts 50 and 56.**

- *Provide IRB approval letters from an IRB that is in compliance with 21 CFR Parts 50 and 56 for each site. Approvals should be updated before study initiation at each site. (Sites will be listed on the CMS website.)*

g. **All aspects of the research study are conducted according to the appropriate standards of scientific integrity.**

- *Describe data safety monitoring procedures.*
- Describe stopping rules.

h. **The research study has a written protocol that clearly addresses, or incorporates by reference, the Medicare standards.**

- *Required of all CED projects.*

i. **The clinical research study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Trials of all medical technologies measuring therapeutic outcomes as one of the objectives meet this standard only if the disease or condition being studied is life-threatening as defined in 21 CFR § 312.81(a) and the patient has no other viable treatment options.**

- *Note: this standard is not relevant to this NCD. No answer required.*

j. **The clinical research study is registered on the www.ClinicalTrials.gov website by the principal sponsor/investigator prior to the enrollment of the first study subject.**

- *Plans to register the study if approved by CMS should be stated. (The ClinicalTrials.gov identifier is required for payment for HSCT)*

k. **The research study protocol specifies the method and timing of public release of all pre-specified outcomes to be measured including release of outcomes if outcomes are negative or study is terminated early. The results must be made public within 24 months of the end of data collection. If a report is planned to be published in a peer-reviewed journal, then that initial release may be an abstract that meets the requirements of the International Committee of Medical Journal Editors. However, a full report of the outcomes must be made public no later than three (3) years after the end of data collection.**

- *Describe your approach to dissemination of the study results.*

l. **The research study protocol must explicitly discuss subpopulations affected by the treatment under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion criteria affect enrollment of these populations, and a plan for the retention and reporting of said populations on the trial. If the inclusion and exclusion criteria are expected to have a negative effect on the recruitment or retention of underrepresented populations, the protocol must discuss why these criteria are necessary. Address the following:**

- *Inclusion and exclusion criteria and how they will affect enrollment.*
- Inclusion of women and minorities.
- Inclusion of Medicare enrollees.

m. **The research study protocol explicitly discusses how the results are or are not expected to be generalizable to the Medicare population to infer whether Medicare patients may benefit from the intervention. Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability or Medicaid eligibility.**

- *Discuss how the methodology addresses the above issues.*

In addition, the prospective clinical study of MRI must include safety criteria for all participants. Such required safety measures for such studies, as further explained in guidance documents from professional societies (e.g., Kanal et al., 2007; Levine et al., 2007), must include but are not limited to:

1. MRI should be done on a case-by-case and site-by-site basis;
2. MRI scan sequences, field intensity, and field(s) of exposure should be selected to minimize risk to the patient while gaining needed diagnostic information for diagnosis or for managing therapy;
3. MRI scanning should be done only if the site is staffed with individuals with the appropriate radiology and cardiology knowledge and expertise on hand;
4. Implanted device patients who are candidates for recruitment for an MRI clinical study should be advised that life-threatening arrhythmias might occur during MRI and serious device malfunction might occur, requiring replacement of the device;
5. Radiology and cardiology personnel and a fully stocked crash cart be readily available throughout the procedure in case a significant arrhythmia develops during the examination that does not terminate with the cessation of the MR study. The cardiologist should be familiar with the patient's arrhythmia history and the implanted device. A programmer that can be used to adjust the device as necessary should be readily available.
6. All such patients should be actively monitored for cardiac and respiratory function throughout the examination. At a minimum, ECG and pulse oximetry should be used. Visual and verbal contact with the patient must be maintained throughout the MRI scan. The patient should be instructed to alert the MRI staff on hand to any unusual sensations, pains, or to any problems.
7. At the conclusion of the examination, the cardiologist should examine the device to confirm that the function is consistent with its preexamination state.
8. Follow-up should include a check of the patient's device at a time remote (1–6 weeks) after the scan to confirm appropriate function.
9. If the implanted device manufacturer has indicated additional safety precautions appropriate for safe MRI performance, these must be included in the study protocol.

Submit the "Required Information," "NCD/CED Coverage Requirements," and study protocol to: Leslye.fitterman3@cms.hhs.gov or

Leslye Fitterman, PhD.
7500 Security Boulevard
Mail Stop S3-02-01
Baltimore, MD 21244-1850

---

[1] "Relative contraindication" is a factor (in this case the presence of an implanted PM) that renders the carrying out of a medical procedure (here, an MRI) generally inadvisable due to potential adverse impact on the patient. However, the risk of harm due to a relative contra-indication to MRI may, in the physician's judgment about a particular patient, be outweighed by expected benefit of information gained from MRI.

Back to Top

Bibliography

Section I - Articles/abstracts cited by requester: with requester's citation numbers:

1. Maisel WH, Moynahan M, Zuckerman BD, et al. Pacemaker and ICD generator malfunctions: analysis of Food and Drug Administration annual reports.[see comment]. *JAMA.* 2006; 295(16): 1901-1906.

2. Rosamond W, Flegal K, Furie K, et al. Heart disease and stroke statistics 2008 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation.* 2008; 117(4): e25-146.

3. Zhan C, Baine WB, Sedrakyan A, Steiner C. Cardiac device implantation in the United States from 1997 through 2004: a population-based analysis. *Journal of General Internal Medicine.* 2008; 23 Suppl 1: 13-19.

4. Kalin R, Stanton MS. Current clinical issues for MRI scanning of pacemaker and defibrillator patients. *Pacing & Clinical Electrophysiology.* 2005; 28(4): 326-328.

5. Kanal E, Barkovich AJ, Bell C, et al. ACR guidance document for safe MR practices: 2007. *AJR* American Journal of Roentgenology. 2007; 188(6): 1447-1474.

6. Levine GN, Gomes AS, Arai AE, et al. Safety of magnetic resonance imaging in patients with cardiovascular devices: an American Heart Association scientific statement from the Committee on Diagnostic and Interventional Cardiac Catheterization, Council on Clinical Cardiology, and the Council on Cardiovascular Radiology and Intervention: endorsed by the American College of Cardiology Foundation, the North American Society for Cardiac Imaging, and the Society for Cardiovascular Magnetic Resonance. *Circulation.* 2007; 116(24): 2878-2891.

7. Roguin A, Schwitter J, Vahlhaus C, et al. Magnetic resonance imaging in individuals with cardiovascular implantable electronic devices. *Europace.* 2008; 10(3): 336-346.

8. Shinbane JS, Colletti PM, Shellock FG. MR in patients with pacemakers and ICDs: Defining the issues. *J Cardiovasc Magn Reson.* 2007; 9(1): 5-13.

9. Cohen J, Costa H, Russo R. Pacemaker and Implantable Cardioverter Defibrillator Safety for Patients Undergoing Magnetic Resonance Imaging (The MagnaSafe Registry). *Journal of the American College of Cardiology.* 2009; 53(10, Supplement 1): A303-A304.

10. Cohen JD, Costa HS, Russo RJ. Abstract 2804: Pacemaker and Implantable Cardioverter Defibrillator Safety for Patients Undergoing Magnetic Resonance Imaging (The MagnaSafe Registry). *Circulation.* 2008 Oct 28; 118(18_MeetingAbstracts): S_778.

11. Del Ojo JL, Moya F, Villalba J, et al. Is magnetic resonance imaging safe in cardiac pacemaker recipients? *Pacing & Clinical Electrophysiology.* 2005; 28(4): 274-278.

12. Gimbel JR, Bailey SM, Tchou PJ, Ruggieri PM, Wilkoff BL. Strategies for the safe magnetic resonance imaging of pacemaker-dependent patients. *Pacing And Clinical Electrophysiology: PACE.* 2005; 28(10): 1041-1046.

13. Gimbel JR, Johnson D, Levine PA, Wilkoff BL. Safe performance of magnetic resonance imaging on five patients with permanent cardiac pacemakers. *Pacing And Clinical Electrophysiology: PACE.* 1996; 19(6): 913-919.

14. Gimbel JR, Kanal E, Schwartz KM, Wilkoff BL. Outcome of magnetic resonance imaging (MRI) in selected patients with implantable cardioverter defibrillators (ICDs). *Pacing And Clinical Electrophysiology: PACE.* 2005; 28(4): 270-273.

15. Martin ET, Coman JA, Shellock FG, Pulling CC, Fair R, Jenkins K. Magnetic resonance imaging and cardiac pacemaker safety at 1.5-Tesla. *Journal Of The American College Of Cardiology.* 2004; 43(7): 1315-1324.

16. Naehle CP, Sommer T, Meyer C, et al. Strategy for safe performance of magnetic resonance imaging on a patient with implantable cardioverter defibrillator. *Pacing & Clinical Electrophysiology.* 2006; 29(1): 113-116.

17. Naehle CP, Strach K, Thomas D, et al. Magnetic resonance imaging at 1.5-T in patients with implantable cardioverter-defibrillators. *Journal of the American College of Cardiology.* 2009; 54(6): 549-555.

18. Naehle CP, Volkert Z, Daniel T, et al. Evaluation of Cumulative Effects of MR Imaging on Pacemaker Systems at 1.5 Tesla. *Pacing and Clinical Electrophysiology.* 2009; 32(12): 1526-1535.

19. Nazarian S, Hansford R, Roguin A, et al. Abstract 2803: Clinical Utility of Magnetic Resonance Imaging of Patients with Permanent Pacemakers and Implantable-Cardioverter Defibrillators at 1.5 Tesla. *Circulation.* 2008 Oct 28; 118(18_MeetingAbstracts): S_777-778.

20. Nazarian S, Roguin A, Zviman MM, et al. Clinical Utility and Safety of a Protocol for Noncardiac and Cardiac Magnetic Resonance Imaging of Patients With Permanent Pacemakers and Implantable-Cardioverter Defibrillators at 1.5 Tesla. *Circulation.* 2006; 114(12): 1277-1284.

21. Sommer T, Naehle CP, Yang A, et al. Strategy for safe performance of extrathoracic magnetic resonance imaging at 1.5 tesla in the presence of cardiac pacemakers in non-pacemaker-dependent patients: a prospective study with 115 examinations. *Circulation.* 2006; 114(12): 1285-1292.

22. Chalela JA, Kidwell CS, Nentwich LM, et al. Magnetic resonance imaging and computed tomography in emergency assessment of patients with suspected acute stroke: a prospective comparison. *The Lancet.* 2007; 369(9558): 293-298.

23. Ge Y. Multiple sclerosis: the role of MR imaging. *AJNR American Journal of Neuroradiology.* 2006; 27(6): 1165-1176.

24. Kidwell CS, Chalela JA, Saver JL, et al. Comparison of MRI and CT for detection of acute intracerebral hemorrhage. *JAMA.* 2004; 292(15): 1823-1830.

25. American College of Radiology. ACR Appropriateness Criteria®: Soft-tissue Masses. Available at: http://www.acr.org/SecondaryMainMenuCategories/quality_safety/app_criteria/pdf/ExpertPanelonMusculoskeletalImaging/SoftTissueMassesDoc19.aspx. Accessed June 16, 2009.

26. American College of Radiology. ACR Appropriateness Criteria®: Ataxia. Available at: http://www.acr.org/SecondaryMainMenuCategories/quality_safety/app_criteria/pdf/ExpertPanelonNeurologicImaging/AtaxiaDoc1.aspx. Accessed June 16, 2009.

27. American College of Radiology. ACR Appropriateness Criteria®: Myelopathy. Available at: http://www.acr.org/SecondaryMainMenuCategories/quality_safety/app_criteria/pdf/ExpertPanelonNeurologicImaging/MyelopathyDoc8.aspx. Accessed June 16, 2009.

28. American College of Radiology. ACR Appropriateness Criteria®: Pre-Irradiation Evaluation and Management of Brain Metastases. Available at: http://www.acr.org/SecondaryMainMenuCategories/quality_safety/app_criteria/pdf/ExpertPanelonRadiationOncologyBrainMetastasesWorkGroup/PreIrradiationEvaluationandManagementofBrainMetastasisDoc3.aspx. Accessed June 16, 2009.

Section II: Additional Citations, Articles Reviewed as Background Information, and Relevant Agency Documents:/p>

Al-Sabagh KH, Christensen BE, Thoergersen AM, et al. Safety of MRI in patients with PM and ICD. Ugeskrift for laeger 2010 Jun 7; 172(23): 1740-4. [Article in Danish]

Barnett HJ, Taylor DW, Eliasziw M, et al. Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. N Engl J Med. 1998; 339(20):1415-1425.

Burke PT, Ghanbari H, Alexander DB, et al. A protocol for patients with cardiovascular implantable devices undergoing MRI: should defibrillation threshold testing be performed post-MRI. J Interv Card Electrophysiol 2010 Jun; 28(1); 59-66.

Endarterectomy for asymptomatic carotid artery stenosis. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. JAMA. 1995; 273(18):1421-1428.

FDA 2010. Executive Summary for March 19, 2010 Circulatory System Devices Panel meeting. Downloaded on August 6, 2010 from: http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/CirculatorySystemDevicesPanel/UCM204715.pdf

Faris OP, Shein M. Food and Drug Administration perspective: Magnetic resonance imaging of pacemaker and implantable cardioverter-defibrillator patients. Circulation. 2006 Sep 19; 114(12): 1232-3. [Editorial]

Gimbel J. Safe, sensible, sagacious: responsible scanning of pacemaker patients. European Heart J. 2005. 26: Online publish-ahead-of-print 9 June 2005.

Götte MJW, Rüssel IK, de Roest GJ, et. al. Magnetic resonance imaging, pacemakers and implantable cardioverter defibrillators: current situation and clinical perspective. Neth Heart J. 2010; 18:31-37.

Hayes DL, Lloyd MA, Friedman PA. Cardiac pacing and defibrillation: A clinical approach. 2000 Futura Publishing Company, Inc.

Hayes DL, Vlietstra RE. Pacemaker malfunction. Ann Intern Med. 1993 Oct 15; 119(8): 828-35.

Hobson RW, 2nd, Weiss DG, Fields WS, et al. Efficacy of carotid endarterectomy for asymptomatic carotid stenosis. The Veterans Affairs Cooperative Study Group. N Engl J Med. 1993; 328(4):221-227.

Mollerus M, Albin G, Lipinski M, Lucca J. Magnetic resonance imaging of pacemaker and implantable cardioverter defibrillators without specific absorption rate restrictions. Europace 2010;12:947-951.

Mollerus M, Albin G, Lipinski M, et al. Cardiac biomarkers in patients with permanent PMs and ICDs undergoing an MR scan. Pacing Clin Electrophysiol 2008 Oct; 31(10); 1241-5.

Mollerus M, Albin G, Lipinski M, et al. Ectopy in patients with permanent PMs and ICDs undergoing an MR scan. Pacing Clin Electrophysiol 2009 June; 32(6): 772-8.

National Collaborating Centre for Chronic Conditions. Stroke. Diagnosis and initial management of acute stroke and transient ischaemic attack (TIA). London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Jul. 37 p. (Clinical guideline; no. 68). (Cited as NICE 2008)

Nazarian A, Halperin HR. How to perform magnetic resonance imaging on patients with implantable cardiac arrhythmia devices. Heart Rhythm 2009 Jan; 6(1): 138-43.

Schmiedel A, Hackenbroch M, Yang A, et al. MRI of the brain in patients with cardiac pacemakers. Experimental and clinical investigations at 1.5 T. RoFo 2005 May: 177(5): 731-44. [Article in German]

Schoenfeld MH. Contemporary Pacemaker and Defibrillator Device Therapy: Challenges Confronting the General Cardiologist. Circulation 2007; 115; 638-53.

Back to Top